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William Henry Perkin

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SULPHOCAMPHYLIC ACID AND ISOLAURONOLIC ACID, WITH REMARKS ON THE CONSTITUTION OF CAMPHOR AND OF SOME OF ITS DERIVATIVES.

BY

W. H. PERKIN, JUN.

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From the Transactions of the Chemical Society, 1898.

Sulphocamphylic Acid and Isolauronolic Acid,* with Remarks on the Constitution of Camphor and of some of its Derivatives.

By W. H. Perkin, jun.

Introduction.

The constitution of camphor still remains unsolved, in spite of the enormous amount of work which has been done during the last few years in almost every conceivable direction.

It is well known that camphor, $C_{10}H_{16}O$, on oxidation, yields *camphoric acid*, $C_8H_{14}(COOH)_2$, and that this acid, on further oxidation, yields *camphanic acid*, $C_8H_{13}(OH)(COOH)_2$, *camphoronic acid*, $C_6H_{11}(COOH)_3$, and other acids containing a smaller number of carbon atoms, but although the constitution of camphoronic acid has now been conclusively proved, there is still very considerable doubt as to the formulæ of camphoric acid and camphanic acid.

That the relationship existing between camphor and camphoric acid is a very close one is proved, not only by the fact that camphoric acid

* Noyes (*Ber.*, 1895, **28**, 549) proposes to alter the name of this acid to *cis*-campholytic acid, and to reserve the name isolauronolic acid for an isomeric acid which he has prepared. As, however, this is likely to cause much confusion, and there seems, in the meantime, no sufficient reason for the change, it has not been adopted in this paper.

is so readily formed by oxidising camphor, but also by the formation of this acid from camphorquinone.

Claisen and Manasse (*Annalen*, 1893, 274—286) showed that camphor is readily converted into isonitrosocamphor, $C_8H_{14}<\begin{matrix}C{:}NOH\\CO\end{matrix}$, by treatment with amylic nitrite and sodium methoxide, and from this compound, by treatment with nitrous acid, they obtained camphorquinone, $C_8H_{14}<\begin{matrix}CO\\CO\end{matrix}$.

From camphorquinone, camphoric acid is readily obtained by the action of a solution of potash in methylic alcohol, hydrolysis and oxidation (due to the oxygen of the air) taking place simultaneously.

$$C_8H_{14}<\begin{matrix}CO\\CO\end{matrix}+H_2O+O \quad = \quad C_8H_{14}<\begin{matrix}COOH\\COOH\end{matrix}.$$

This series of simple reactions fully confirms the view, which has long been held by chemists, that camphor contains the group $-CH_2\cdot CO-$, and that when it is converted into camphoric acid, this group is oxidised to two carboxyl groups.

$C_8H_{14}<\begin{matrix}CH_2\\CO\end{matrix}$. Camphor.

$C_8H_{14}<\begin{matrix}COOH\\COOH\end{matrix}$. Camphoric acid.

It follows, therefore, that the constitution of camphor could be readily deduced from the constitution of camphoric acid, and this accounts for the great number of experiments which have been carried out with this acid.

Bredt's suggestion (*Ber.*, 1893, **26**, 3049), that camphoronic acid has the constitution

$$\begin{matrix}(CH_3)_2C\cdot COOH\\ |\\CH_3\cdot C\cdot CH_2\cdot COOH\\ |\\COOH\end{matrix}$$

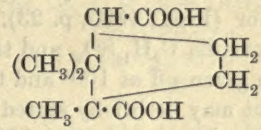
was the first great advance in elucidating the formula of camphoric acid, and now that this constitution of camphoronic acid has been proved by the synthesis of the acid (Perkin and Thorpe, Trans., 1897, **71**, 1169), it can be stated with certainty that camphoric acid, $C_{10}H_{16}O_4$, contains 9 of its carbon atoms grouped in the following way.

$$\begin{matrix}(CH_3)_2C-C\\ |\\CH_3\cdot C-C\cdot C.\\ |\\C\end{matrix}$$

This fact disposes of a number of formulæ which had been suggested for camphoric acid, such as those of V. Meyer and Ballo, and of Tiemann,

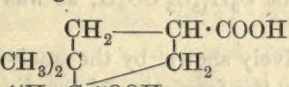
but, on the other hand, it does not afford a sufficient basis on which to build up a constitution for camphoric acid that shall not be open to question.

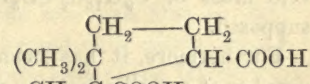
Arguing from the formula of camphoronic acid, Bredt (*loc. cit.*, p. 3049) has suggested that camphoric acid is probably represented thus.



and this well-known formula does undoubtedly explain a very large number of the reactions of the acid in a comparatively simple manner.

The investigation of sulphocamphylic acid and of isolauronolic acid, on which the author of this paper has been engaged during the last nine years, has, however, brought to light some facts which it seems almost impossible to explain with the aid of Bredt's formula, and this led the author, in 1896 (Proc., 1896, p. 191*), to suggest that the constitution of camphoric acid might equally well be represented by the following formulæ.

I. 

II. 

An acid having either of these formulæ could, on oxidation, yield camphoronic acid quite as well as an acid of the constitution suggested by Bredt.

It will furthermore be shown that the results obtained in the investigation of isolauronolic acid can only be readily explained on the assumption that formula I is the correct expression for the constitution of camphoric acid, and for this reason this formula has been adopted in this paper.

Among the many remarkable reactions in the camphor group, one of the most interesting is certainly the decomposition which takes place when camphoric acid is gently heated with concentrated sulphuric acid, the camphoric acid being converted almost quantitatively into *sulphocamphylic acid*, with evolution of carbonic oxide.

$$C_{10}H_{16}O_4 + H_2SO_4 = C_9H_{14}SO_5 + CO + 2H_2O.$$

This decomposition was first observed by Walter (*Ann. Chim. Ph.*, 1843, [iii], 9, 177), and subsequently investigated by Kachler (*Ann-*

* There is an unfortunate printer's error (in the abstract) in the first of these formulæ, two hydrogen atoms having been omitted.

alen, 1873, **169**, 179) and Damsky (*Ber.*, 1887, **20**, 2959), and for many years the formula for crystallised sulphocamphylic acid was supposed to be $C_9H_{16}SO_6 + 2H_2O$, a formula by which it is represented in the last edition of Beilstein's *Handbuch* (vol. i, p. 905).

During the course of further experiments on this acid, it was, however, clearly proved by Koenigs and Meyer (*Ber.*, 1894, **27**, 3466), as well as by the author (Proc., 1895, p. 23), that sulphocamphylic acid in reality has the formula $C_9H_{14}SO_5$, and that it crystallises with $3H_2O$, two of which are given off at 100° and the third at about 110°, and the proof of this fact may be briefly stated as follows.

When the silver salt of sulphocamphylic acid is treated with methylic iodide, the dimethylic salt is obtained, and this, on analysis, was shown to have the formula $C_9H_{12}SO_5(CH_3)_2$ (Koenigs and Meyer, *loc. cit.*, p. 3467).

Similarly, the potassium salt of sulphocamphylic acid, when treated with phosphorus pentachloride or pentabromide, yields the *sulphochloride or sulphobromide*, and these, on analysis, give numbers agreeing sharply with the formulæ $C_9H_{13}O_2(SO_2Cl)$ and $C_9H_{13}O_2(SO_2Br)$, formulæ which clearly prove that the composition of sulphocamphylic acid must be $C_9H_{13}O_2{\cdot}SO_3H$, and not $C_9H_{15}O_3{\cdot}SO_3H$, as was at first supposed.

Furthermore, it has been conclusively shown by the analysis of a number of metallic salts, as well as by the formation of the dimethylic salt mentioned above, that sulphocamphylic acid is dibasic, and therefore its formula may be written $C_8H_{12}(SO_3H){\cdot}COOH$.

The investigation of the sulphochloride and sulphobromide of sulphocamphylic acid has given very interesting results, some of which are described in this paper; others are reserved for a future communication.

The sulphochloride* is a beautiful, crystalline substance, which melts at 168°, and is at the same time decomposed with evolution of sulphur dioxide and formation of a new acid, $C_8H_{12}Cl{\cdot}COOH$, melting at 106°.

$$C_8H_{12}(SO_2Cl){\cdot}COOH = C_8H_{12}Cl{\cdot}COOH + SO_2.$$

This acid has been called *chlorodihydro-β-camphylic acid*, because, on prolonged treatment with alcoholic potash, it is converted into β-camphylic acid,† with elimination of hydrogen chloride,

$$C_8H_{12}Cl{\cdot}COOH = C_8H_{11}{\cdot}COOH + HCl.$$

* The decompositions described here are exactly similar to those which Kipping and Pope (Trans., 1895, **67**, 371) have used with such success in the preparation of π-halogen derivatives of camphor.

† Compare Proc., 1893, 109; 1895, 23; 1896, 189. A detailed description of this very interesting acid will, it is hoped, form the subject of a future communication.

In a similar manner, the sulphobromide of sulphocamphylic acid, when heated above its melting point, decomposes, with evolution of sulphur dioxide and formation of *bromodihydro-β-camphylic acid*, and this acid is decomposed by alcoholic potash in the same way as the corresponding chloro-acid, yielding again β-camphylic acid.

$C_8H_{12}(SO_2Br)\cdot COOH$	$\rightarrow$	$C_8H_{12}Br\cdot COOH$	$\rightarrow$	$C_8H_{11}\cdot COOH.$
Sulphobromide.		Bromodihydro-β-camphylic acid.		β-Camphylic acid.
M. p. 150°		129°		105°

Since, then, it is clear from the above that sulphocamphylic acid must be represented by the formula $C_8H_{12}(SO_3H)\cdot COOH$, the next important matter is to discuss all the evidence which has a bearing on the further arrangement of the atoms in this molecule.

It has been frequently found in the camphor and terpene series that the study of the behaviour of these substances and their derivatives towards oxidising agents has given valuable clues to their constitution, and in the case of sulphocamphylic acid also, although in a less degree than might have been expected, important results have been obtained in this way.

Kachler (*Annalen*, 1873, **169**, 181), who was the first to oxidise sulphocamphylic acid, found that, when heated with nitric acid, it is converted into oxalic acid and a beautifully crystalline tribasic acid, which he called *sulphopimelic acid*, and the formation of which he expressed by the equation

$$C_9H_{16}SO_6 + O_6 = C_7H_{12}SO_7 + C_2H_2O_4 + H_2O.$$

Subsequently, Koenigs and Hoerlin (*Ber.*, 1893, **26**, 2045) carefully investigated this sulphopimelic acid, and found that at 160—170° it is decomposed with evolution of sulphur dioxide and formation of terebic acid; they therefore considered that Kachler's acid must be sulphoisopropylsuccinic acid, in which case the formation of terebic acid is readily understood.

$$(CH_3)_2\underset{SO_3H}{C}\cdot CH(COOH)\cdot CH_2\cdot COOH = (CH_3)_2\underset{O}{C}\cdot CH(COOH)\cdot \underset{CO}{CH_2} + SO_2 + H_2O$$

Sulphoisopropylsuccinic acid.* Terebic acid.

These chemists also found that small quantities of dimethylmalonic acid, $(CH_3)_2C(COOH)_2$, are produced during the oxidation of sulphocamphylic acid with nitric acid, an important result, since the formation of this acid indicates that sulphocamphylic acid contains the group $-C\cdot C(CH_3)_2\cdot C-$.

* In studying the possible formulæ for sulphocamphylic acid, it is very difficult to understand how the sulphonic group in sulphopimelic acid can occupy the position given to it here.

Sulphocamphylic acid is also readily oxidised by potassium permanganate in alkaline solution, yielding a variety of very interesting products, which have been carefully investigated by the author of this paper, but the description of these must be reserved for a future communication.

Action of Heat on Sulphocamphylic Acid. Formation of Isolauronolic Acid, $C_8H_{13}\cdot COOH$.

When sulphocamphylic acid is heated in small quantities, or distilled with superheated steam, it undergoes a very remarkable decomposition, yielding isolauronolic acid and sulphuric acid (Koenigs and Hoerlin, *Ber.*, 1893, **26**, 813 ; Perkin, *Centralblatt.*, 1893, ii, 50),

$$C_9H_{14}SO_5\cdot H_2O = C_8H_{13}\cdot COOH + H_2SO_4,$$

but, unfortunately, at the high temperature necessary for the decomposition, the sulphuric acid formed destroys much of the sulphocamphylic acid, and the yield of isolauronolic acid obtained hardly ever exceeds 10 per cent. of the theoretical. It was subsequently discovered by the author that isolauronolic acid may be obtained in comparatively large quantities by fusing sulphocamphylic acid in a cast iron pot with caustic soda, a remarkable result, which may be explained as follows.

In the first place, the sulphocamphylic acid is decomposed by the fusion with soda, with formation of the sodium salts of the isomeric *α*- and *β*-camphylic acids, $C_8H_{11}\cdot COOH$ (Perkin, Proc., 1893, 109 ; 1895, 23).

$$C_8H_{12}(SO_3H)\cdot COOH + 3NaOH = C_8H_{11}\cdot COONa + Na_2SO_3 + 3H_2O.$$

The iron of the vessel in which the fusion is carried out then reduces these sodium salts, and the product, which is coloured dark brown by the ferric oxide which it holds in suspension, contains the sodium salt of isolauronolic acid.

$$\underset{\text{Sodium } \alpha\text{- and } \beta\text{-camphylates.}}{C_8H_{11}\cdot COONa} + 2H = \underset{\text{Sodium isolauronolate.}}{C_8H_{13}\cdot COONa}.$$

Although this method is a considerable improvement on the dry distillation of sulphocamphylic acid, it is, nevertheless, a very laborious process, and the best way for preparing isolauronolic acid is undoubtedly that worked out by Blanc (*Bull. Soc. Chim.*, [iii], **15**, 1191), which consists in treating a solution of camphoric anhydride in chloroform with aluminium chloride, when the following remarkable decomposition takes place.

$$C_{10}H_{14}O_3 = C_8H_{13}\cdot COOH + CO.$$

Another method of formation of isolauronolic acid direct from camphoric acid, to be discussed later in this paper, is that discovered by Walker (Trans., 1893, **63**, 495). Walker submitted orthoethylic sodium camphorate to electrolysis, and obtained in this way, besides ethylic campholytate, an isomeric ethylic salt boiling at 135—140° (15mm.), which he first called diethylic camphothetate, but which was subsequently (Trans., 1895, **67**, 347) shown to be the ethylic salt of isolauronolic acid.

Lastly, Noyes (*Ber.*, 1894, **65**, 917; 1895, **67**, 549) has obtained isolauronolic acid by the following series of reactions.

The imide of camphoric acid, $C_8H_{14}\begin{matrix}CO\\CO\end{matrix}>NH$, when treated with potash, yields *β-camphoraminic acid*, $C_8H_{14}(CONH_2)\cdot COOH$, and this, by the action of sodium hypobromite, is converted into *dihydroaminocampholytic acid*, $C_8H_{14}(NH_2)\cdot COOH$; nitrous acid converts this amido-acid into Walker's *campholytic acid*, which, when boiled with dilute sulphuric acid, undergoes molecular change, yielding isolauronolic acid.

The determination of the constitution of isolauronolic acid is of great importance, for the following reasons.

1. It is formed from camphoric anhydride by elimination of CO.
2. It is formed from sulphocamphylic acid by heat.
3. It is reconverted into sulphocamphylic acid by treatment with sulphuric acid (see p. 835).

From these facts, it will be seen that isolauronolic acid is closely related to camphoric acid on the one hand, and to sulphocamphylic acid on the other, so that the determination of the constitution of this acid must throw much light on the question of the constitution of camphoric and of sulphocamphylic acids.

Oxidation of Isolauronolic Acid. Formation of Isolauronic Acid, $C_9H_{12}O_3$.

If a drop of potassium permanganate solution is added to a solution of isolauronolic acid in dilute sodium carbonate, the colour is instantly discharged, even at 0°; and, on investigating this reaction, it is found that the first product of the oxidation is an acid of the formula $C_9H_{12}O_3$.

$$C_9H_{14}O_2 + 2O = C_9H_{12}O_3 + H_2O.$$

This new acid, which was first described by Koenigs and Meyer (*Ber.*, 1894, **27**, 3467), and called by them *isolauronic acid*, melts at 133°, and differs from isolauronolic acid in being readily soluble in hot water; it is a ketonic acid, and forms the following well characterised derivatives.

Oxime	$COOH\cdot C_7H_{11}\cdot C{:}NOH$	m. p. 222°
Semicarbazone.....	$COOH\cdot C_7H_{11}\cdot C{:}N\cdot NH\cdot CONH_2$	„ 248
*Phenylhydrazone**	$COOH\cdot C_7H_{11}\cdot C{:}N\cdot NH\cdot C_6H_5$	„ 199

Oxidation of Isolauronic Acid.—Although stable to permanganate at temperatures below 0°, isolauronic acid is readily oxidised by this agent at ordinary temperatures, as also by a mixture of potassium dichromate and sulphuric acid at 90—95°, the principal substances formed being

γ-Dimethylacetylbutyric acid, $CH_3\cdot CO\cdot C(CH_3)_2\cdot CH_2\cdot CH_2\cdot COOH$.

a-Dimethylglutaric acid, $COOH\cdot C(CH_3)_2\cdot CH_2\cdot CH_2\cdot COOH$.

a-Dimethylsuccinic acid, $COOH\cdot C(CH_3)_2\cdot CH_2\cdot COOH$.

All these substances afford important evidence as to the constitution of isolauronic acid, but there can be no doubt, as will be shown later, that it is the first named which is especially valuable in this connection.

Acetyldimethylbutyric acid is identical with the acid which Tiemann (*Ber.*, 1895, **28**, 2176) obtained by the oxidation of *β*-dihydroxydihydrocampholenic acid, and which he named dimethyl-3-hexanon-2 acid.

That this acid has the constitution

$$CH_3\cdot CO\cdot C(CH_3)_2\cdot CH_2\cdot CH_2\cdot COOH,$$

is proved by the following considerations.

1. It is a ketonic acid, as is shown by the fact that it yields a well characterised oxime and semicarbazone.

2. When reduced with sodium amalgam, it is converted into a lactone, $CH_3\cdot \underset{O}{CH}\cdot C(CH_3)_2\cdot CH_2\cdot \underset{CO}{CH_2}$ (b. p. 239—241°), a fact which indicates that the CO group is either in the γ- or δ- position.

3. Sodium hypobromite readily reacts with the acid, with separation of bromoform and formation of *aa-dimethylglutaric acid*,

$$COOH\cdot C(CH_3)_2\cdot CH_2\cdot CH_2\cdot COOH;$$

this shows that the ketonic acid contains the group $CH_3\cdot CO$. The dimethylglutaric acid formed in this way melts at 84°, and is isomeric with *ββ*-dimethylglutaric acid, $COOH\cdot CH_2\cdot C(CH_3)_2\cdot CH_2\cdot COOH$ (m. p. 101°; Goodwin and Perkin, Trans., 1896, **69**, 1473), and since on oxidation the former yields *aa*-dimethylsuccinic acid,

$$COOH\cdot C(CH_3)_2\cdot CH_2\cdot COOH,$$

it can only have the constitution $COOH\cdot C(CH_3)_2\cdot CH_2\cdot CH_2\cdot COOH$

4. From the formula of *aa*-dimethylglutaric acid, two ketonic acids, $C_8H_{14}O_3$, may be derived, namely,

I. $CH_3\cdot CO\cdot C(CH_3)_2\cdot CH_2\cdot CH_2\cdot COOH$;

II. $COOH\cdot C(CH_3)_2\cdot CH_2\cdot CH_2\cdot CO\cdot CH_3$;

* Carl Meyer (*Inaugural Dissertation Munich*, 1895, p. 38).

but there can be no doubt that formula I represents the constitution of the acid obtained from isolauronic acid, because throughout the whole camphor series there is overwhelming evidence that the three methyl groups contained in this substance and its derivatives are united to neighbouring carbon atoms forming the complex

$$CH_3 \cdot C—C(CH_3)_2,$$

a condition which is satisfied by formula I, but not by II.

Reduction of Isolauronic Acid to Dihydroisolauronic Acid, $C_7H_{11} \cdot CH(OH) \cdot COOH$.

The action of sodium amalgam on isolauronic acid was first investigated by Carl Meyer (*Dissertation Munich*, 1895, p. 45) who obtained in this way two products.

1. A lactone, $C_9H_{14}O_2$, melting at 47—50° and yielding on hydrolysis a hydroxy-acid melting at 143°.

2. An acid melting at 81° which does not yield a lactone, and which, on analysis, gave the following numbers.

Found (mean of three analyses) C = 62·95 ; H = 8·66.
$C_9H_{14}O_3$ requires C = 63·53 ; H = 8·23.
$C_9H_{16}O_3$ „ C = 62·71 ; H = 9·30.

These results led Meyer to conclude that the acid melting at 81° was a mixture of two acids, $C_9H_{14}O_3$ and $C_9H_{16}O_3$, which could not be separated by crystallisation.

As the investigation of the behaviour of isolauronic acid on reduction is a matter of fundamental importance in determining the constitution of this acid, a great many experiments on this subject have been made by the author, the results of which differ considerably from those obtained by Carl Meyer. In the first place, Carl Meyer's experiments were repeated exactly as he described them, using isolauronic acid which had been very carefully purified by repeated crystallisation, but no trace of a solid lactone could be detected in the product, which consisted of a beautifully crystalline acid melting at 88—89°, and on analysis gave numbers agreeing sharply with those required by the formula $C_9H_{14}O_3$.

Found (mean of two analyses) C = 63·36 ; H = 8·21.
$C_9H_{14}O_3$ requires C = 63·53 ; H = 8·23.

The conditions of reduction were then varied, but in all cases it was found that the isolauronic acid had been converted almost quantitatively into the acid $C_9H_{14}O_3$, which, since it is formed by the addition of two atoms of hydrogen to isolauronic acid, has been called *dihydroisolauronic acid.*

The solution of dihydroisolauronic acid in sodium carbonate does

not decolorise permanganate except on long standing, showing that the acid is a saturated acid, and this is confirmed by the fact that the acid does not combine with bromine, or with hydrogen bromide, and that it is not further reduced even when its alkaline solution is boiled with sodium amalgam.

Since dihydroisolauronic acid is formed by the reduction of the ketonic acid isolauronic acid, it is evident that it must be a hydroxy-acid, and the next important point was to determine whether it was capable of forming a lactone, since, in this way, valuable evidence as to the relative positions of the hydroxyl and carboxyl groups, and indirectly as to the position of the CO and COOH in isolauronic acid, might be obtained.

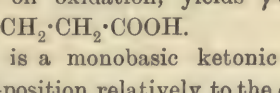
This matter has been most carefully investigated, but it was not found possible to obtain even traces of a lactone by boiling the hydroxy-acid with dilute sulphuric acid; and, indeed, the hydroxy-acid may be distilled without decomposition; it may therefore be safely stated that *dihydroisolauronic acid is incapable of forming a lactone.*

This statement may, at first sight, appear to be at variance with the results obtained by Carl Meyer (*Dissertation*, p. 46), who, by the reduction of isolauronic acid, obtained, as mentioned above, small quantities of a lactone, $C_9H_{14}O_2$, melting at 47—50°, and which on hydrolysis yielded an acid melting at 143°. The principal product of the reduction was, however, a hydroxy-acid melting at 81°, and yielding on analysis numbers agreeing with those required by a mixture of acids, $C_9H_{14}O_3$ and $C_9H_{16}O_3$, and there can now be no doubt that this acid was simply slightly impure dihydroisolauronic acid (m. p. 88°). Since Meyer's acid melting at 81° was isolated from the product of the reduction of isolauronic acid after this had been boiled with dilute acids, it is evident that his acid is also incapable of forming a lactone, and in this respect Meyer's experiments agree with those of the author. With regard to the nature of the lactone melting at 47—50° and yielding, on hydrolysis, the acid melting at 143°, it seems extremely probable that this was *campholactone*, $C_9H_{14}O_2$, which melts at 50—51°, and which on hydrolysis with baryta yields *campholactonic acid*, $C_9H_{16}O_3$, melting at 143°;* the few properties of his lactone which Meyer mentions confirm this view. Since, however, campholactone is the lactone corresponding to lauronolic acid (see p. 815), it is exceedingly difficult to understand its formation by the reduction of a derivative of isolauronolic acid.

* According to Woringer (*Annalen*, 1885, **227**, 10) campholactonic acid is precipitated as an oil on acidifying the solution of its barium salt; the author, however, in conjunction with Mr. R. W. Collinson, has obtained the acid by this method in the form of beautiful prismatic crystals melting at 143°. An account of this interesting acid is reserved for a future communication.

The Constitution of Isolauronolic Acid, of Isolauronic Acid, and of Sulphocamphylic Acid, with remarks on the Constitution of Camphor and of Camphoric Acid.

It has already been stated that, in the opinion of the author, the results obtained in this investigation can best be explained on the assumption that camphoric acid has the constitution represented by the formula



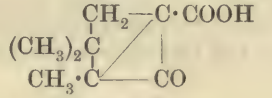
and in giving the reasons for this statement it will be best in the first place to discuss the constitution of isolauronic acid, in doing which the principal points to be borne in mind are,

1. Isolauronic acid, on oxidation, yields γ-dimethylacetylbutyric acid, $CH_3 \cdot CO \cdot C(CH_3)_2 \cdot CH_2 \cdot CH_2 \cdot COOH$.

2. Isolauronic acid is a monobasic ketonic acid containing the ketonic group in the β-position relatively to the carboxyl group. This is proved by the fact that the dihydroisolauronic acid obtained by its reduction is incapable of forming a lactone.

3. Since dihydroisolauronic acid distils unchanged, it cannot contain the group $-\overset{|}{C}H \cdot CH(OH)-$, because acids containing that group, on distillation, lose water with formation of the corresponding unsaturated acids. Isolauronic acid itself must, therefore, contain the group $COOH \cdot \overset{\diagdown\diagup}{C} \cdot CO \cdot \overset{\diagdown\diagup}{C}$, the free bonds of which must all be united to carbon.

From the formula of camphoric acid given above an expression for the constitution of isolauronic acid can be easily deduced which will satisfy these conditions and explain all the known properties of the acid, namely,

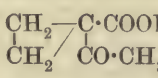


Isolauronic acid.

This formula, which appears to the author to be the only possible formula for isolauronic acid, represents the acid as a β-ketonic acid, and to this the objection might be raised that the acid gives no coloration with ferric chloride, and that when heated it does not decompose with evolution of carbon dioxide. The reply to the first objection is that β-ketonic acids, or their ethereal salts, which have both α-hydrogen atoms replaced by radicles do not appear to give a coloration with ferric chloride, thus, for example, the author finds that ethylic dimethylacetoacetate, $CH_3 \cdot CO \cdot C(CH_3)_2 \cdot COOC_2H_5$, does not give a coloration with ferric chloride.

The relatively great stability of isolauronic acid is also quite easily explained. The ease with which β-ketonic acids are decomposed by heat or alkalis with elimination of carbon dioxide depends very much on their constitution.

Thus acetoacetic acid, $CH_3 \cdot CO \cdot CH_2 \cdot COOH$, and methylacetoacetic acid, $CH_3 \cdot CO \cdot CH(CH_3) \cdot COOH$, are oils which decompose slowly at ordinary temperatures with evolution of carbon dioxide, whereas dimethylacetoacetic acid, $CH_3 \cdot CO \cdot C(CH_3)_2 \cdot COOH$, is solid, and although still very easily decomposed, it is distinctly more stable than the other two acids. These three acids are furthermore readily decomposed in the same manner by boiling with potash. When, however, the carboxyl and acetyl groups in such compounds are attached to a closed chain, as in the case of acetyltrimethylenecarboxylic acid,

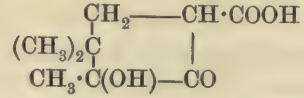


an acid which has a somewhat similar formula to that suggested for isolauronic acid, the stability of the molecule may be, but is not always, enormously increased. Acetyltrimethylenecarboxylic acid, for example, may be boiled with potash for hours without decomposition, and the free acid is only slowly decomposed into carbon dioxide and acetyltrimethylene even at 180—200°.

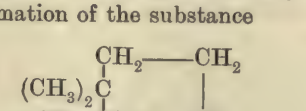
If, then, the introduction of one closed chain into the molecule can bring about such an extraordinary change in stability, it is not remarkable that this stability should be still more pronounced in a substance like isolauronic acid, the formula of which is represented above, not only as containing two closed chains, but also as having no α-hydrogen atoms.

The formation of dimethylacetylbutyric acid from isolauronic acid may be readily explained with the aid of this formula as follows.

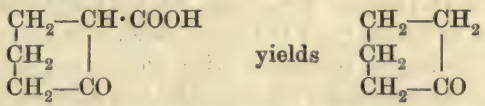
In the first place, the trimethylene ring is split with the addition of the elements of water and formation of an intermediate substance of the formula



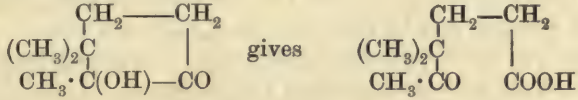
and this being a β-ketonic acid with one α-hydrogen atom not replaced, may be assumed to decompose readily with evolution of carbon dioxide and formation of the substance



Thus Dieckmann (*Ber.*, 1894, 27, 103) has shown that ethylic β-ketopentamethylenecarboxylate, a substance of very similar constitution to the "intermediate" substance, is readily and quantitatively decomposed on hydrolysis, with formation of ketopentamethylene.



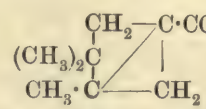
Lastly, the ketonic substance of the formula given above, being produced in the presence of oxidising agents, is readily converted into acetyldimethylbutyric acid.



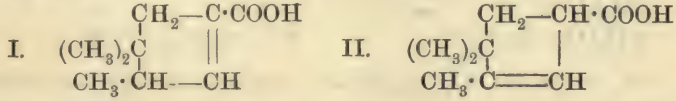
Assuming that the constitution given to isolauronic acid is correct, the next point is to deduce from this the formula for isolauronolic acid. This at first sight seems to be a simple matter, since isolauronic acid is formed from isolauronolic acid by replacing two hydrogen atoms by an oxygen atom, thus.

$$\underset{\text{Isolauronolic acid.}}{C_9H_{14}O_2} + 2O = \underset{\text{Isolauronic acid.}}{C_9H_{12}O_3} + H_2O,$$

and therefore the formula for isolauronolic acid, which suggests itself at once, is



But this formula would represent isolauronolic acid as a saturated acid, and yet in many of its properties it behaves like an unsaturated acid, so that there are grounds for assuming that one of the alternative formulæ



is more probable.

It must, however, be remembered that it is sometimes a matter of the greatest difficulty to distinguish between unsaturated substances and trimethylene derivatives, since the latter frequently form additive compounds with bromine, hydrogen bromide, and, less readily, with hydrogen; but trimethylene derivatives are, as a rule, stable towards permanganate at ordinary temperatures.

In favour of the unsaturated formula for isolauronolic acid is undoubtedly the fact that this acid instantly reduces permanganate in alkaline solution even at 0°, that it forms a dibrom-additive product when its solution in chloroform is treated with bromine at 0° and in the dark (Noyes, *Ber.*, 1895, **28**, 552), and that it combines with hydrogen bromide;* on the other hand, it is only reduced with difficulty by prolonged treatment with boiling amylic alcohol and sodium, remaining unchanged when its alkaline solution is boiled with sodium amalgam.

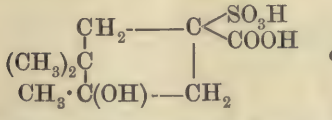
But the chief argument against the trimethylene formula is this, that this formula does not explain the fact that isolauronolic acid is obtained from sulphocamphylic acid by the action of heat, and is again converted into this acid by treatment with sulphuric acid.

It seems probable that the latter most interesting formation of sulphocamphylic acid takes place in two stages.

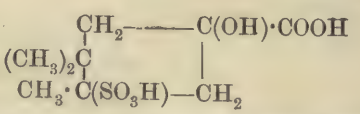
$$\underset{\text{Isolauronolic acid.}}{C_9H_{14}O_2} + H_2SO_4 = \underset{\text{Intermediate substance.}}{C_9H_{16}SO_6}.$$

$$C_9H_{16}SO_6 = \underset{\text{Sulphocamphylic acid.}}{C_9H_{14}SO_5} + H_2O.$$

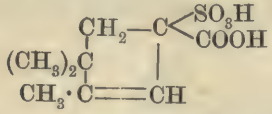
Assuming, then, that isolauronolic acid contains a trimethylene ring, the addition of sulphuric acid can only take place by the splitting of the trimethylene ring, and we shall then get for the formula of the intermediate substance either



or



and the constitution of sulphocamphylic acid deduced from these formulæ would be either



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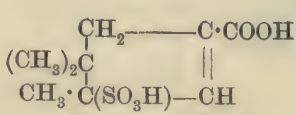
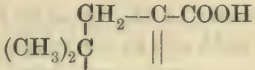


If, now, we remove SO_3 from these formulæ to produce isolauronolic acid, we can quite easily see that the acid may have one of the two unsaturated formulæ given on p. 808, but the reconstruction of the trimethylene formula by eliminating SO_3 involves an intramolecular change for the occurrence of which little probability exists.

If, then, isolauronolic acid is an unsaturated acid, the question at once arises whether its constitution is represented by formula I or II (p. 808), and there can be no doubt that the former, that is, the formula

* Noyes (private communication).

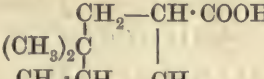


Isolauronolic acid.

best explains the properties of this acid.

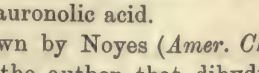
Isolauronolic acid distils without decomposition, and when boiled with dilute sulphuric acid does not yield a lactone. It cannot, therefore, be a $\beta\gamma$-unsaturated acid such as is represented in formula II, since an acid of this constitution would readily yield a lactone under these conditions; and other properties of this acid, which are explained in more detail in the following pages, lead to the same conclusion, namely, that isolauronolic acid is an $\alpha\beta$-unsaturated acid.

Perhaps the most striking confirmation of this view of the constitution of isolauronolic acid is the following. When reduced by amylic alcohol and sodium, isolauronolic acid, $C_9H_{14}O_2$, yields dihydroisolauronolic acid, $C_9H_{16}O_2$, the double bond being reduced, and it is obvious that the constitution of this acid will be represented by the formula

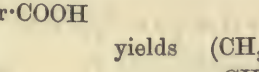


quite independently of whether formula I or II (p. 808) is taken as the constitution of isolauronolic acid.

But it has been shown by Noyes (*Amer. Chem. J.*, 1896, **18**, 689), and independently by the author, that dihydroisolauronolic acid, on bromination, behaves quite normally, and yields a monobromo-derivative in which the bromine atom is doubtless in the α-position. Now, when this bromo-derivative is treated with alcoholic potash, isolauronolic acid is quantitatively produced, hydrogen bromide being eliminated between the α- and β-carbon atoms in the usual way.

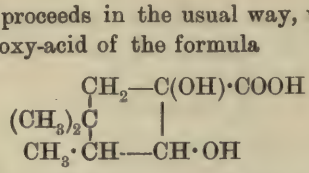


But it must be confessed that, although this formula is so very satisfactory in many ways, it is not quite easy to deduce from it the formula for isolauronic acid which was advocated on p. 806, namely,

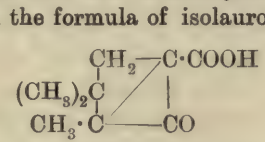


It is, of course, possible to do this by assuming that the oxidation of isolauronolic acid by permanganate takes place in the following stages.

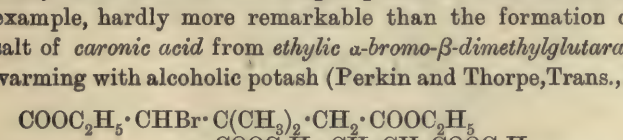
I. The oxidation proceeds in the usual way, with formation of the intermediate dihydroxy-acid of the formula



II. The CH·OH group is oxidised to CO, and at the same time water is eliminated, and the trimethylene ring is formed, these changes resulting in the formula of isolauronic acid,



The formation of a trimethylene ring in this way, during the course of an oxidation, is certainly unusual; but there are grounds for assuming that the trimethylene ring may be produced much more easily than used to be thought possible. The above change is, for example, hardly more remarkable than the formation of the *ethylic* salt of *caronic acid* from *ethylic α-bromo-β-dimethylglutarate*, by simply warming with alcoholic potash (Perkin and Thorpe, Trans., 1897, p. 107).



It has already been shown that it is improbable that the relationship existing between isolauronolic acid and sulphocamphylic acid can be explained on the basis of the trimethylene formula, and it remains to be shown that, with the aid of the unsaturated formula for isolauronolic acid, this difficulty can be got over.

Sulphocamphylic acid is formed, as is well-known, by the action of sulphuric acid on camphoric acid or camphoric anhydride,

$$C_{10}H_{16}O_4 + H_2SO_4 = C_9H_{14}SO_5 + CO + 2H_2O,$$

and it is also produced quantitatively when isolauronolic acid is warmed with concentrated sulphuric acid,

$$C_9H_{14}O_2 + H_2SO_4 = C_9H_{14}SO_5 + H_2O.$$

If it be remembered that camphoric anhydride is readily converted into isolauronolic acid with evolution of carbon monoxide when its solution in chloroform is treated with aluminium chloride in the cold, it seems very probable that, in the formation of sulphocamphylic acid from camphoric anhydride, isolauronolic acid is first produced, and that this then reacts with the sulphuric acid.

The formation of sulphocamphylic acid in this way may be assumed to take place in two stages.

In the first place, the sulphuric acid is added on at the double bond in the isolauronolic acid, a change which may take place in two ways, with the formation of the following substances.

I. $CH_2—C(OH)\cdot COOH$ / $(CH_3)_2C$ | $CH_3\cdot CH—CH\cdot SO_3H$

II. $CH_2—C(SO_3H)\cdot COOH$ / $(CH_3)_2C$ | $CH_3\cdot CH—CH\cdot OH$

The large excess of sulphuric acid which it is necessary to have present, then acts as a dehydrating agent, water is eliminated, and thus two expressions of the constitution of sulphocamphylic acid are obtained, namely,

I. $CH_2—C\cdot COOH$ / $(CH_3)_2C$ || $CH_3\cdot CH—C\cdot SO_3H$

II. $CH_2—C(SO_3H)\cdot COOH$ / $(CH_3)_2C$ | $CH_3\cdot C=CH$

Since, however, the elimination of SO_3 and formation of isolauronolic acid can only be explained by the aid of formula I, this view of the constitution of sulphocamphylic acid has been adopted in this paper. This formula is also in accord with all the known reactions of sulphocamphylic acid, thus, for example, it represents the substance as being an unsaturated acid, and this accounts for the fact that the acid is at once oxidised by permanganate in alkaline solution even at temperatures considerably below 0°.

From the above, it will be seen that the formation and properties of isolauronic, isolauronolic, and sulphocamphylic acids, can be explained with the aid of the author's formula for camphoric acid, and it remains to be shown that the other possible formulæ for camphoric acid, namely, Bredt's formula I and the formula II,

I. $CH—COOH$ (ortho) / $(CH_3)_2C$ CH_2 / $CH_3\cdot C—COOH$ (allo) CH_2

II. $CH_2—CH_2$ / $(CH_3)_2C$ $CH\cdot COOH$ (ortho) / $CH_3\cdot C—COOH$ (allo)

which was at one time considered probable by the author (Proc., 1896, p. 191), do not give an explanation of the formation and properties of these acids.

In the formation of isolauronolic acid from camphoric acid, by the action of sulphuric acid or aluminum chloride, the elements of formic acid are eliminated,

$$C_8H_{12}(COOH)_2 = C_8H_{13}\cdot COOH + H\cdot COOH,$$

or, in other words, one of the carboxyl groups in the camphoric acid is removed, and the important point is to determine which of the two carboxyl groups remains.

In order to do this, it will be convenient to adopt the nomenclature used by Brühl, Walker, and others, and to represent the carboxyl groups as *ortho* and *allo* in the way shown in the above formulæ.

Now there are two series of unsaturated acids which can be obtained from camphoric acid by the elimination of formic acid, according to whether the ortho- or the allo-carboxyl group is removed during the process, namely.

1. The series the chief member of which is lauronolic acid $C_8H_{13}\cdot COOH$.

2. The series the chief member of which is isolauronolic acid $C_8H_{13}\cdot COOH$.

And it can be proved that the former series contain the *allo*- the latter the *ortho*-carboxyl group of the original camphoric acid molecule.

In order to make this clear, it will be necessary to refer briefly to Walker's and Walker and Henderson's important researches on the electrolysis of the sodium and potassium salts of the ethylic ortho- and allo-camphorates (Trans., 1893, **63**, 495; 1895, **67**, 337; 1896, **69**, 748). Camphoric acid yields two isomeric sodium ethylic salts which may be provisionally represented by the formulæ

$$C_8H_{14}\begin{cases}COOC_2H_5\ (ortho)\\COONa\ (allo)\end{cases} \qquad C_8H_{14}\begin{cases}COONa\ (ortho)\\COOC_2H_5\ (allo)\end{cases}$$

Sodium ethylic orthocamphorate. *Sodium ethylic allocamphorate.*

The first of these is formed by the addition of sodium ethoxide to camphoric anhydride,

$$C_8H_{14}\begin{cases}CO\\CO\end{cases}O + \begin{matrix}C_2H_5\\|\\ONa\end{matrix} = C_8H_{14}\begin{cases}COOC_2H_5\\COONa\end{cases},$$

and the second by the partial hydrolysis of ethylic camphorate,

$$C_8H_{14}\begin{cases}COOC_2H_5\\COOC_2H_5\end{cases} + NaOH = C_8H_{14}\begin{cases}COONa\\COOC_2H_5\end{cases} + C_2H_5\cdot OH.$$

When sodium ethylic *ortho*-camphorate is electrolysed, the product is found to contain the ethereal salts of two isomeric unsaturated acids of the formula $C_8H_{13}\cdot COOH$; one of these acids is isolauronolic acid, and the other has been named campholytic acid. Campholytic acid combines directly with bromine, yielding a dibromide, $C_8H_{13}Br_2\cdot COOH$, and this when treated with sodium carbonate is decomposed with formation of a bromo-derivative of an unsaturated hydrocarbon,

$$C_8H_{13}Br_2\cdot COONa = C_8H_{13}Br + CO_2 + NaBr,$$

and since this decomposition is shown only by the dibrom-additive products of $\alpha\beta$-unsaturated acids, Walker concludes that campholytic acid contains the group

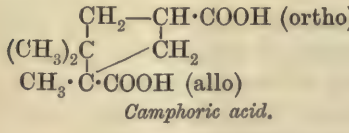
$$-CH_2-C\overset{\diagup\!\!\diagdown}{=\!=}C-$$
$$\quad\quad\quad

When camphanic acid * is distilled, it readily loses carbon dioxide and yields campholactone,

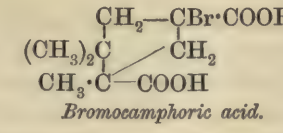
$$C_8H_{13}(COOH)<\begin{matrix}O\\|\\CO\end{matrix} = C_8H_{14}<\begin{matrix}O\\|\\CO\end{matrix} + CO_2.$$

In this decomposition, the carboxyl group which is eliminated must be the *ortho-* one, since lactone formation cannot take place between a hydroxy-group and a carboxyl group when both are attached to the same carbon atom. Now lauronolic acid is readily converted into campholactone by boiling with dilute sulphuric acid, and therefore in its formation from bromocamphoric anhydride as represented above, it is clear that the carboxyl group which is removed is also the *ortho-* one, or in other words lauronolic acid contains the *allo*-carboxyl group of the original camphoric acid molecule.

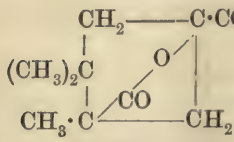
Taking the author's formula for camphoric acid as the basis, it will be seen at once that these changes are all easily understood, the following formulæ representing the constitution of the various substances mentioned above.



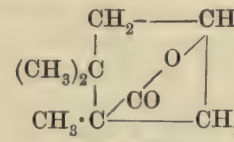
Camphoric acid.



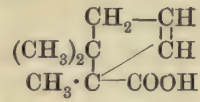
Bromocamphoric acid.



Camphanic acid.



Campholactone.



Lauronolic acid.

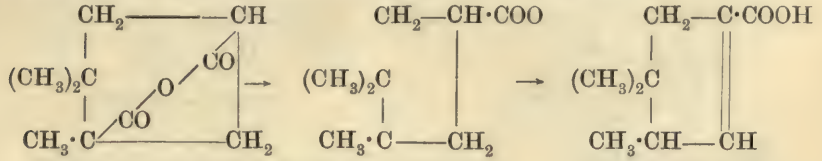
The formula for lauronolic acid is in accordance with Walker's views, in so far that it represents this acid as a $\beta\gamma$-unsaturated acid, and thus accounts for the ease with which it is converted into campholactone on treatment with acid; and since allo-campholytic acid also readily yields campholactone with acids, it is very probable, as stated above, that it is stereoisomeric with lauronolic acid.

In a similar manner, the constitution of isolauronolic acid (and of campholytic acid) may be deduced from the author's camphoric acid

* Lauronolic acid is also produced in this decomposition

$$C\,H_{13}(COOH)<\begin{matrix}O\\|\\CO\end{matrix} = C_8H_{13}\cdot COOH + CO_2.$$

formula, either by considering the formation of this acid from sodium ethylic *ortho*-camphorate by electrolysis, or from camphoric anhydride by the action of aluminium chloride. In the latter case, the acid is formed simply by the elimination of CO from the *allo*-position, and thus leads to an intermediate formula, which, by necessary molecular rearrangement, gives without difficulty the formula for isolauronolic acid.



Camphoric anhydride. *Isolauronolic acid.*

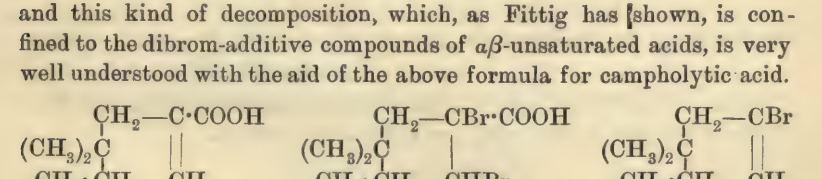
It will be noticed that the formula for isolauronolic acid given here is identical with that which was deduced for this acid on p. 810.

This formula appears to agree well with the known properties of isolauronolic acid; it represents the acid, for example, as an $\alpha\beta$-unsaturated acid, and thus accounts for the fact that it is not converted into a lactone on boiling with dilute acids.

Isolauronolic acid is formed when campholytic acid is boiled with dilute acids, and it is therefore probable, as mentioned before, that these two acids are stereoisomeric. Now campholytic acid, $C_9H_{14}O_2$, yields a dibromide, $C_9H_{14}Br_2O_2$, which, when treated with sodium carbonate, gives a bromo-derivative of an unsaturated hydrocarbon (see p. 813),*

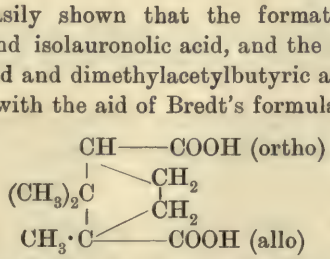
$$C_8H_{13}Br_2\cdot COONa = C_8H_{13}Br + CO_2 + NaBr,$$

and this kind of decomposition, which, as Fittig has shown, is confined to the dibrom-additive compounds of $\alpha\beta$-unsaturated acids, is very well understood with the aid of the above formula for campholytic acid.



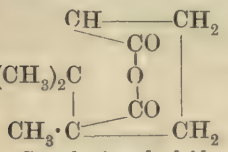
Campholytic acid and isolauronolic acid. *Dibromide.* *Bromo-derivative of hydrocarbon.*

It may be easily shown that the formation and properties of lauronolic acid and isolauronolic acid, and the oxidation of the latter to isolauronic acid and dimethylacetylbutyric acid, cannot be satisfactorily explained with the aid of Bredt's formula for camphoric acid.



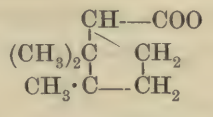
Isolauronolic acid seems to behave in the same way (Noyes, *Ber.*, 1895, **28**, 552).

If, in proof of this statement, we take the formation of isolauronolic acid by the action of aluminium chloride on camphoric anhydride, a reaction which, as was shown on p. 816, takes place with elimination of CO from the allo-position, we obtain the following result.



Camphoric anhydride. (Bredt.)

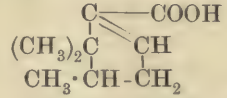
gives



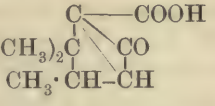
Intermediate formula.

This intermediate formula must now undergo intramolecular change, and the only possible formula for isolauronolic acid which can be derived from this, and at the same time represent the acid as an $\alpha\beta$-unsaturated acid, is I, and if from this formula we now endeavour to deduce the constitution of isolauronic acid, $C_9H_{12}O_3$ (p. 806), we get the expression II,

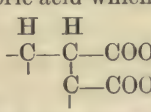
I.

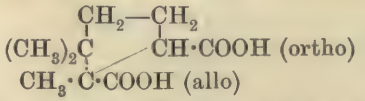


II.



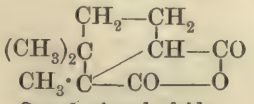
which does not account at all for the properties of this acid, and with the aid of which it seems quite impossible to imagine the formation of dimethylacetylbutyric acid, $CH_3 \cdot CO \cdot C(CH_3)_2 \cdot CH_2 \cdot CH_2 \cdot COOH$, by further oxidation.

There is still one formula for camphoric acid which must be discussed, especially as it contains the group  , which Walker (Trans., 1896, 59, 757), as the result of his investigations, considers must be present in this acid, and that is the formula.

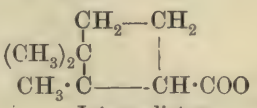


This formula was suggested by the author some time since (Proc., 1896, 191) as possibly being the correct expression for the constitution of camphoric acid.

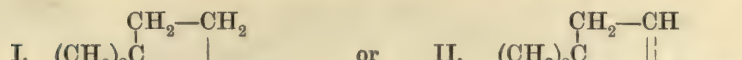
Using the same arguments as before, the formation of isolauronolic acid from this formula would be expressed thus.



Camphoric anhydride.

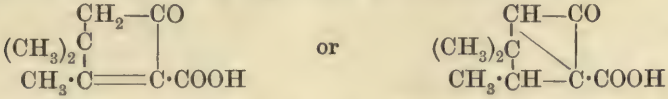


Intermediate.

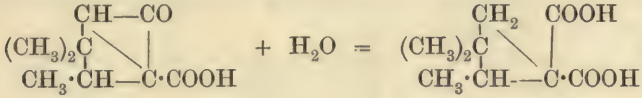


Isolauronolic acid.

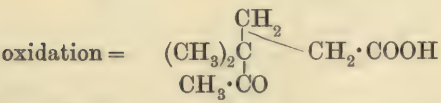
These views of the constitution of isolauronolic acid, although much more satisfactory than those derived from Bredt's formula, are nevertheless improbable, since they would lead to formulæ such as



for isolauronic acid, which do not satisfy the condition 3 stated on p. 806. The first of these also could not give acetyldimethyl butyric acid on oxidation, and although the formation of this acid acid might be explained with the aid of the second formula, if it is assumed that the following changes could take place,

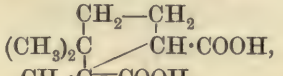


Intermediate.



this assumption is highly improbable, since the intermediate trimethyltetramethylenedicarboxylic acid represented here would be a very stable substance, easily capable of isolation, and very difficult to attack by oxidising agents.

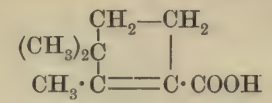
There are also other arguments against the formula,



for camphoric acid, such as, for example, the difficulty in explaining the lactone nature of camphanic acid, which appear to the author to make it much less probable than the formula adopted in this paper.

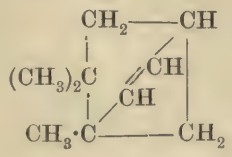
In a paper published a short time since (*Bull. Soc. Chim.*, 1898, [iii], 19, 534), G. Blanc starting with the formula * given just above for camphoric acid, deduces the expression

* This formula, which Blanc calls Bouveault's formula, for camphoric acid was first suggested by the author of this paper (Proc., 1896, 191); Bouveault's communication did not appear till later (compare *Centralblatt*, 1897, ii, 856).



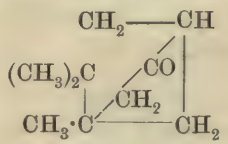
for isolauronolic acid, and states that this may be taken as "fixée avec la *plus absolue certitude.*" Blanc arrives at this formula (which is identical with that given on p. 818) from the consideration that, as isolauronolic acid is inactive, the asymmetry of the two asymmetric carbon atoms in camphoric acid must have disappeared in the formation of this acid, and he also explains that this formula readily accounts for the formation of acetyldimethylbutyric acid on oxidation.

The results of the examination of the ethylic and methylic salts of isolauronolic acid, which are given on p. 833, make it appear probable that this acid is feebly dextrorotatory,* and in this respect it resembles borneocamphene, which is very feebly dextrorotatory. But, since borneocamphene gives camphoric acid on oxidation, it probably still contains *both* the asymmetric carbon atoms of the original camphor molecule, and its formula, on the basis of the camphor formula given on p. 798, may be represented as



It is well known that comparatively small changes in the structure of a substance often very much affect its rotation, and arguments as to constitution based on optical inactivity are useless until it is satisfactorily proved that the substance in question is really inactive and not merely a racemoid modification.

If the views expressed in this paper are correct, the constitution of camphor will be represented by the formula



which, as will be shown in a future paper, appears to account satisfactorily for the reactions of this substance.

This research was commenced in 1889 in the laboratories of the Heriot Watt College, Edinburgh, and since 1892 it has been continued in the Owens College, Manchester. During the course of the

* In order to decide this point, very careful experiments on the acid itself are in progress.

work, the author has received valuable assistance from Messrs. B. Prentice, W. H. Bentley, E. Haworth, J. L. Heinke, C. T. Abell, F. H. Lees, and others; he is also much indebted to Professors F. S. Kipping and James Walker for reading the manuscript and criticising the theoretical conclusions arrived at in the Introduction to this paper, and also to Prof. Ossian Aschan for valuable suggestions.

The author also wishes to state that the greater part of the heavy expense which is unavoidable in an investigation of this kind has been met by repeated Grants from the Research Fund of the Royal Society, without which it would hardly have been possible to have carried on these experiments.

Experimental.

Sulphocamphylic acid, $(CH_3)_2\begin{matrix}CH_2—C\cdot COOH\\ |\quad\quad\quad ||\\ CH_3\cdot CH—C\cdot SO_3H\end{matrix}$

In preparing small quantities of this acid, Koenigs and Hoerlein (*Ber.*, 1893, **26**, 812) heated 20 grams of camphoric acid with 40 c.c. of sulphuric acid for 4—5 hours on a water bath, and after adding water and extracting the unchanged camphoric acid with ether, they evaporated to the crystallising point and purified the crude sulphocamphylic acid by recrystallisation from ethylic acetate. This process gives very good results, but it is not well adapted for preparing the acid in such quantities as were required for the present investigation; and after many experiments, the following method was devised, by which large quantities of sulphocamphylic acid may be obtained in an almost pure condition in a comparatively short time. Five hundred grams of camphoric acid * and 1250 grams of concentrated sulphuric acid are heated in a large, round-bottomed flask on a briskly boiling water bath, when the crystals rapidly dissolve with evolution of much carbon monoxide, which must be carefully led away through a tube into the draught hole of a good draught cupboard, or, better still, into the open air. After 6—7 hours heating, the thick, brown liquid is left until cold, and then mixed with an equal volume of water, and allowed to stand overnight to crystallise, when the whole generally sets to a solid cake. The crystals, which consist of crude sulphocamphylic acid, are collected with the aid of the pump, and freed as far as possible from the dark mother liquors by pressure; these mother liquors were always discarded, as, although by suitable treatment an appreciable amount of

* The whole of the camphoric acid used in this research was obtained from Kahlbaum, and it was always found to be of very excellent quality.

sulphocamphylic acid may be extracted from them, the process is tedious and the product difficult to purify.

The crude acid obtained from two or three such operations is transferred to a large earthenware pot, and after being mixed with five times its weight of water, steam is passed in until the temperature has been raised to the boiling point and the whole has dissolved. On standing for 24 hours in a cool place, the greenish liquid deposits a quantity of unchanged camphoric acid, which is removed by filtration through canvas bags, and the filtrate is then mixed with a little animal charcoal, and steam again passed in until the boiling point is reached. After filtering through large folded filters, the solution of sulphocamphylic acid will be nearly colourless; it is now concentrated considerably on the water bath and extracted about eight times with ether, so as to free it completely from unchanged camphoric acid. The solution, after being evaporated to a small bulk, deposits the sulphocamphylic acid, on standing, as a mass of colourless prisms, which, after removal of the mother liquor with the pump, is almost pure; in this form, it was used in the experiments described in this paper. For the analyses, the acid was once more crystallised from water, and allowed to remain exposed to the air at the ordinary temperature to dry.

Determination of the water of crystallisation.

0·9663 of the air dried crystals lost, at 95°, 0·1162 = 12·03 per cent.
0·7247 „ „ „ 95°, 0·0891 = 12·29 „
0·8101 of the crystals, dried at 95°, lost, at 130°, 0·0610 = 7·53 per cent.
0·6356 „ „ „ „ 130°, 0·0454 = 7·11 „

$C_9H_{14}SO_5,3H_2O$ losing $2H_2O$ = 12·49 per cent.
$C_9H_{14}SO_5,H_2O$ „ H_2O = 7·14 „

Analysis of the anhydrous acid.

0·1266 gave 0·2147 CO_2 and 0·0689 H_2O. C = 46·25; H = 6·04.
0·1520 „ 0·2587 CO_2 „ 0·0827 H_2O. C = 46·41; H = 6·04.
0·6794 „ 0·6653 $BaSO_4$. S = 13·45.
0·6098 „ 0·6002 $BaSO_4$. S = 13·51.

$C_9H_{14}SO_5$ requires C = 46·15; H = 5·98; S = 13·68 per cent.

These results show that sulphocamphylic acid has the formula $C_9H_{14}SO_5 + 3H_2O$, and not $C_9H_{16}SO_6 + 2H_2O$, as was supposed by Kachler and others to be the case, and of the 3 molecules of water 2 are given off at 95° and the remaining molecule at 130°.

Sulphocamphylic acid crystallises from water, in which it is excessively soluble, in large, colourless, glistening prisms. Its general properties have already been mentioned in the Introduction to this paper, and many of its derivatives are described in detail in the following pages.

Salts of Sulphocamphylic Acid.

Hydrogen Potassium Sulphocamphylate, $C_9H_{13}SO_5K + H_2O$(?).—This salt was prepared by dissolving sulphocamphylic acid in water, dividing the solution into two parts, neutralising the one with pure potassium carbonate, and then adding the other. It is readily soluble in water, and crystallises in magnificent tabular crystals which do not become opaque on exposure to the air, and do not lose weight at 100°. When dry, this salt has the appearance of alabaster, and breaks up into flakes on pounding in a mortar. Analysis.

0·4305 gram of the salt gave 0·1320 K_2SO_4. K = 13·76.

$C_9H_{13}SO_5K + H_2O$ requires K = 13·45.

$C_9H_{13}SO_5K$ requires K = 14·33.

From the results of this analysis, it is possible that this salt crystallises with $1H_2O$.

Potassium Sulphocamphylate, $C_9H_{12}SO_5K_2$.—Considerable quantities of this salt were prepared during the experiments on sulphocamphylic chloride (p. 823) by exactly neutralising an aqueous solution of sulphocamphylic acid with potassium carbonate, and then concentrating on the water bath. The mass of colourless crystals which separated on standing was collected with the aid of the pump, rapidly washed with small quantities of water, and drained on a porous plate. The air dried salt does not appear to contain water of crystallisation, since the loss at 150° only amounted to 0·8 per cent.

0·4328, dried at 150°, gave 0·2493 K_2SO_4 ; K = 25·82.

$C_9H_{12}SO_5K_2$ requires K = 25·16.

This salt crystallises in small needles, and is very readily soluble in water.

Hydrogen Sodium Salt, $C_9H_{13}SO_5Na + 5H_2O$.—This salt was accidentally prepared during the course of some experiments on the action of sodium hydrogen sulphite on sulphocamphylic acid ; a very strong solution of the acid was nearly neutralised with sodium carbonate, and then a saturated solution of sodium hydrogen sulphite was added. On standing, a quantity of iridescent plates separated, which were collected and purified by recrystallisation from water. The crystals, after being allowed to stand on a porous plate exposed to the air for 3 days, were analysed.

I. 0·5556 gram, heated at 100° for 2½ hours, lost 0·1156 H_2O = 20·8 per cent., and the residue, on treatment with sulphuric acid, gave 0·1196 Na_2SO_4. Na = 6·98 per cent.

II. 0·4490 gram, heated at 100° until constant, lost 0·0901 H_2O =

20·28 per cent. This salt very probably has the formula $C_9H_{13}SO_5Na + 5H_2O$, which contains 6·65 per cent. of sodium, and when heated at 100° it loses $4H_2O$ or 20·81 per cent. of water.

Besides these salts, Koenigs and Hoerlin (*Ber.*, 1893, **26**, 813) prepared and analysed the *neutral silver salt*, $C_9H_{12}Ag_2SO_5 + 2H_2O$, the *hydrogen silver salt*, $C_9H_{13}AgSO_5 + 2H_2O$, and a beautifully crystalline *hydrogen lead salt*, $(C_9H_{13}SO_5)_2Pb + 6H_2O$.

Carl Meyer (*Dissertation Munich*, 1895, p. 25) also prepared the *methylic salt*, $C_9H_{12}SO_5(CH_3)_2$ (m. p. 72°), and a *hydrogen methylic salt*, $C_9H_{13}SO_5{\cdot}CH_3$ (m. p. 140°).

Sulphocamphylic Chloride, $C_8H_{12}(COOH){\cdot}SO_2Cl$.

This substance is formed when dry potassium sulphocamphylate is treated with phosphorus pentachloride. When mixed under ordinary conditions, these two compounds reacted with considerable violence, much heat was developed, and the whole became converted into a carbonaceous mass from which nothing crystalline could be extracted, and for a long time all attempts to prepare sulphocamphylic chloride were unsuccessful.

Ultimately, however, by working at low temperatures, and mixing the substances in small portions at a time, so as to avoid, as far as possible, rise of temperature, it was found possible to isolate sulphocamphylic chloride in sufficient quantities to allow of its properties being carefully investigated. The method of preparation and extraction employed is as follows.

Phosphorus pentachloride (100 grams) is weighed out into a narrow beaker containing a thermometer, and cooled by a freezing mixture to at least −10°, and carefully dried potassium sulphocamphylate (40 grams) is then gradually added in quantities of about 2 grams at a time, the whole being rapidly stirred with the thermometer after each addition, great care being taken during the operation that the temperature does not rise above 0°. When all the potassium salt has been added, the beaker is left in an ice chest overnight, and the dark brown, almost black, product is then stirred with powdered ice; after standing for about an hour, the dark, insoluble precipitate is collected, washed with water, and allowed to remain in contact with porous porcelain in a cool place until quite dry. The almost black product thus obtained is now ground up with sand, transferred to a Soxhlet apparatus, and extracted with dry ether, when the whole of the sulphochloride passes into the ether, leaving a large quantity of an insoluble, black residue. If the brown, ethereal solution is evaporated in a flask to a small bulk, and the flask loosely corked, and allowed to stand in an ice chest, crude sulphocamphylic chloride separates in brown crusts, which may

be obtained almost colourless by repeated recrystallisation from ether with the aid of animal charcoal.

0·1994 gave 0·1124 AgCl. Cl = 13·93.

$C_8H_{12}(COOH)\cdot SO_2Cl$ requires Cl = 14·05 per cent.

Sulphocamphylic chloride melts at 168°, with decomposition. It is readily soluble in alcohol and warm acetic acid, but only sparingly in benzene and light petroleum, and crystallises beautifully either from dilute acetic acid or from dilute alcohol. It dissolves in cold sodium carbonate solution, and may be reprecipitated unchanged on the addition of acids; if, however, the alkaline solution is warmed for a few minutes, the sulphochloride is converted into sulphocamphylic acid, and no precipitation takes place on acidifying.

Chlorodihydro-β-camphylic Acid, $C_8H_{12}Cl\cdot COOH$.

When strongly heated, sulphocamphylic chloride readily undergoes decomposition, with elimination of sulphur dioxide and formation of *chlorodihydro-β-camphylic acid*, thus,

$$C_8H_{12}(SO_2Cl)\cdot COOH = C_8H_{12}Cl\cdot COOH + SO_2.$$

In investigating this decomposition, pure sulphocamphylic chloride, in quantities of about 10 grams, was heated under reduced pressure in a small retort connected with a long glass air condenser* until the evolution of sulphur dioxide had ceased; on rapidly distilling the residue, almost the whole passed over at 195—200° (45 mm.) as a light greenish oil, which, on cooling, solidified completely. The solid distillate, which consisted of almost pure chlorodihydro-β-camphylic acid, was dissolved in boiling light petroleum (b. p. 50—60°), filtered, and the solution allowed to cool slowly, when beautiful, colourless needles were gradually deposited which, on analysis, gave the following numbers.

0·1354 gave 0·2852 CO_2 and 0·0870 H_2O. C = 57·44; H = 7·14.
0·2044 „ 0·1480 AgCl. Cl = 17·92.
0·2225 „ 0·1651 AgCl. Cl = 18·36.
$C_8H_{12}Cl\cdot COOH$ requires C = 57·32; H = 6·9. Cl = 18·78 per cent.

Chlorodihydro-β-camphylic acid melts at 105—106°, and is readily soluble in alcohol, ether, chloroform, acetic acid, and warm light

* In carrying out this operation, it is necessary to use a condenser at least 2 feet long, and to avoid, as far as possible, narrow openings in connecting the apparatus with the vacuum pump, as during the decomposition the chlorodihydrocamphylic acid is carried over by the sulphur dioxide to such an extent as to readily block up the connections and cause an explosion.

petroleum, but almost insoluble in water; it is best crystallised from light petroleum or from dilute acetic acid.

It dissolves in dilute sodium carbonate solution without decomposition, and the cold solution instantly decolorises permanganate, but the experiments on this oxidation hitherto made have not given very definite results. The solution of the acid in chloroform does not decolorise bromine, even on long standing, and the acid does not appear to react with hydrogen bromide at ordinary temperatures, since its solution in glacial acetic acid, after being saturated with hydrogen bromide and kept for some days, deposits the unchanged substance when evaporated over potash in a vacuum desiccator.

In chlorodihydro-β-camphylic acid the chlorine is very firmly held, as is shown by the fact that, even if the solution of the acid in sodium carbonate is left in contact with excess of sodium amalgam, very little reduction takes place; if, however, the acid is boiled with sodium amalgam, reduction does take place, with formation of substances which are at present under investigation.

Dibromo-chlorodihydro-β-camphylic acid, $C_8H_{12}Br_2Cl\cdot COOH$.

The action of bromine on chlorodihydro-β-camphylic acid was investigated in order to show that this substance is unsaturated, and thus to obtain indirect evidence of the unsaturated nature of sulphocamphylic acid. Bromine appears to have little action on the solution of chlorodihydrocamphylic acid in chloroform, and although the dry halogen reacts readily, a good deal of hydrogen bromide is evolved, and considerable difficulty was experienced in isolating the product. This was ultimately accomplished as follows. The finely powdered acid, in quantities of half a gram, was exposed on a watch-glass in a desiccator containing bromine and sulphuric acid for about $1\frac{1}{2}$ hours, until the substance had become coloured red throughout by the bromine, care being taken to remove the watch-glass before the mass commenced to become liquid. The product was left exposed to the air until the excess of bromine had evaporated, and the sticky residue was then ground up in a mortar several times with small quantities of light petroleum (b. p. 40—50°); about half of it dissolved, leaving a residue which was very sparingly soluble in light petroleum. This may be recrystallised from dilute alcohol if the operation is rapidly performed, and in this way beautiful, glistening prisms are obtained which gave the following results on analysis.

0·1656 gave 0·1910 CO_2 and 0·0576 H_2O. C = 31·45; H = 3·86.

$C_8H_{12}Br_2Cl\cdot COOH$ requires C = 30·99. H = 3·73 per cent.

0·1342 gram gave 0·1995 gram of the mixed chloride and bromide of

silver, the amount required by the formula $C_8H_{12}Br_2Cl\cdot COOH$ being 0·1994 gram.

Dibromochlorodihydro-β-camphylic acid decomposes rapidly at about 171—172°. It is readily soluble in alcohol, benzene, chloroform, and acetic acid, almost insoluble in cold light petroleum, and, as stated above, it may be recrystallised from dilute alcohol if the operation be rapidly performed, otherwise the acid decomposes, with formation of a substance, not yet investigated, which melts at about 100—102° and decomposes with evolution of gas at 150—160°.

Dibromochlorodihydrocamphylic acid dissolves in dilute caustic soda, and the solution, on gently warming, rapidly deposits bromoform; if this be removed and the aqueous solution acidified, an oily acid separates which, on standing, gradually solidifies.

β-Camphylic Acid, $C_8H_{11}\cdot COOH$.

This acid is formed when chlorodihydro-β-camphylic acid is digested with alcoholic potash, hydrogen chloride being eliminated according to the equation

$$C_8H_{12}Cl\cdot COOH = C_8H_{11}\cdot COOH + HCl.$$

The pure acid was dissolved in a little alcohol, the solution heated to boiling in a reflux apparatus, and then a large excess of strong alcoholic potash added in small quantities at a time; decomposition takes place slowly, with separation of potassium chloride. After boiling for 2 hours, water was added, the solution evaporated until free from alcohol, cooled well, and acidified with hydrochloric acid, when an almost colourless, crystalline acid separated; this, after recrystallisation from dilute acetic acid, melted at 103—105°, and on examination proved to be β-camphylic acid.

0·1505 gave 0·3896 CO_2 and 0·1064 H_2O. C = 70·60; H = 7·85.
$C_8H_{11}\cdot COOH$ requires C = 71·05; H = 7·89 per cent.

β-camphylic acid has been obtained in quantity by the fusion of sulphocamphylic acid with caustic soda, and a detailed description of the properties, and the discussion of the constitution of this interesting substance, is reserved for a future communication.

Sulphocamphylic Bromide, $C_8H_{12}(COOH)\cdot SO_2Br$.

This can be prepared by treating dry potassium sulphocamphylate with phosphorus pentabromide, the reaction being much less violent than is the case with phosphorus pentachloride (p. 823). The dry potassium salt (16 grams) is gradually mixed in a mortar with the pentabromide (60 grams), when a vigorous action sets in, torrents of

hydrogen bromide are evolved, and the mass becomes quite pasty. After standing for 2 hours, the product is stirred with powdered ice until the crude sulphobromide has become quite hard, the whole is then collected, and the ochre-coloured precipitate washed well with water, and dried on a porous plate at the ordinary temperature. The product is purified by recrystallisation from ether, exactly as in the case of the corresponding sulphochloride, and the sample employed for analysis was also recrystallised from dilute alcohol.

0·1598 gave 0·2120 CO_2 and 0·0603 H_2O. C = 36·18; H = 4·20.
0·1846 „ 0·1146 AgBr. Br = 26·45.
$C_8H_{12}(COOH)SO_2Br$ requires C = 36·36; H = 4·37. Br = 26·93 per cent.

When heated in a capillary tube, sulphocamphylic bromide softens at about 147° and melts at 150° with decomposition, due to elimination of sulphur dioxide. It is readily soluble in alcohol and in boiling benzene, but only sparingly in the latter solvent, and also in ether or light petroleum in the cold.

Bromodihydro-β-camphylic Acid, $C_8H_{12}Br{\cdot}COOH$.

At temperatures slightly above its melting point, sulphocamphylic bromide decomposes rapidly with evolution of sulphur dioxide and formation of *bromodihydro-β-camphylic acid*; but at the same time a quantity of carbonaceous matter is formed, and unless care is taken in carrying out the decomposition, it is almost impossible to extract the product and obtain it in a crystalline condition. The best results were obtained in the following way. Test tubes containing each about 2 grams of sulphocamphylic bromide were gradually heated in a sulphuric acid bath until the temperature reached 155°, when decomposition rapidly set in, with evolution of sulphur dioxide. After remaining for a few seconds at this point, the temperature was allowed to sink to about 140°, and kept at this until no more sulphur dioxide was evolved.

If the uninviting-looking, black, tarry product be now digested with light petroleum (b. p. 60°) the brominated acid will be extracted, the tarry impurity remaining undissolved, and the yellow solution, on standing in flat basins at the ordinary temperature, deposits ochre-coloured, crystalline crusts as the solvent gradually evaporates.

The crude product was purified by recrystallisation from dilute formic acid, with the aid of animal charcoal, an operation which must be rapidly carried out, as prolonged boiling with the formic acid decomposes the substance.

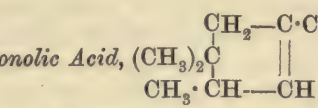
The pale, ochre-coloured, crystalline precipitate, which separates

from the hot formic acid solution on rapidly cooling and stirring with a glass rod, gave the following results on analysis.

0·1518 gave 0·2580 CO_2 and 0·0775 H_2O. C = 46·35 ; H = 5·67.
0·2050 ,, 0·1648 AgBr. Br = 34·18.
$C_8H_{12}Br{\cdot}COOH$ requires C = 46·34 ; H = 5·57 ; Br = 34·33 per cent.

Bromodihydro-β-camphylic acid melts at 128—129°, and when heated rapidly in small quantities, distils with very little decomposition. It dissolves readily in alcohol, benzene, acetic acid, and ether, but is only sparingly soluble in light petroleum. When digested with alcoholic potash, it behaves in the same way as chlorodihydro-β-camphylic acid, yielding β-camphylic acid.

Isolauronolic Acid,



The isolauronolic acid required for this research was nearly all prepared by the two following methods.

I. *The Action of Heat on Sulphocamphylic Acid.*—When rapidly heated, crystallised, air dried sulphocamphylic acid is decomposed into isolauronolic acid and sulphuric acid, according to the equation

$$C_8H_{12}(SO_3H){\cdot}COOH,H_2O = C_8H_{13}{\cdot}COOH + H_2SO_4.$$

Unfortunately, at the temperature of the reaction the sulphuric acid formed decomposes much of the product, so that the yield of isolauronolic acid actually obtained is not more than 8—10 per cent. of the theoretical. The decomposition of sulphocamphylic acid was carried out under reduced pressure in small retorts connected by rubber joints with a long air condenser fitting into an ordinary distilling flask, the latter being connected with the water pump. On heating the sulphocamphylic acid (10 grams), the mass froths up without actually melting, and becomes black at a comparatively low temperature, white fumes coming over which partially condense in the condenser tube in beautiful, feathery groups like snow crystals, and partially pass over into the receiver in the form of an oil which rapidly solidifies. The distillation is stopped when oil ceases to come over ; and the retort, which is filled with a voluminous mass of carbon, is replaced by a fresh one. It was found best to distil the acid in quantities of not more than ten grams, as, if larger quantities are employed, the frothing, which is always most troublesome, becomes unmanageable.

The product, which smells strongly of sulphur dioxide and oil of turpentine, is dissolved in ether, the ethereal solution separated from

the water present, dried over calcium chloride, evaporated, and the solid residue, which contains oily impurity, allowed to remain in contact with porous porcelain until dry and nearly colourless. The crude isolauronolic acid thus obtained is then very easily purified by recrystallisation, either from dilute alcohol or from dilute acetic acid, from which solvents it separates in the form of beautiful, glistening prisms which melt at 133—135°. The analysis gave the following results.

I. 0·1455 gave 0·3726 CO_2 and 0·1203 H_2O. C = 69·89 ; H = 9·18.
II. 0·1160 „ 0·2984 CO_2 „ 0·0961 H_2O. C = 70·16 ; H = 9·19.
$C_8H_{13}\cdot COOH$ requires C = 70·13 ; H = 9·09 per cent.

II. *Fusion of Sulphocamphylic Acid with Caustic Soda in Cast Iron Pots.*—When fused in cast iron vessels with caustic soda, sulphocamphylic acid undergoes a remarkable decomposition, yielding isolauronolic acid in considerable quantities, a reaction which, as explained in the introduction to this paper, evidently takes place in the following two stages.

In the first place, the sodium salts of α- and β-camphylic acids* are formed.

$$C_8H_{12}(SO_3Na)\cdot COONa + NaOH = C_8H_{11}\cdot COONa + Na_2SO_3 + H_2O,$$

and these salts are then reduced by the iron of the cast iron vessel, with formation of the sodium salt of isolauronolic acid,

$$C_8H_{11}\cdot COONa + 2H = C_8H_{13}\cdot COONa.$$

As this reaction was employed for preparing the greater portion of the isolauronolic acid used in this research, the following description of the process is given in detail.

Caustic soda (450 grams), mixed with about 250 c.c. of water in the outer vessel of an ordinary large glue-pot, is heated on a Fletcher ring burner until dissolved, and sulphocamphylic acid (150 grams) is added in small quantities at a time, and with constant stirring ; the temperature is then raised slowly to about 240°, and maintained at that point for 45 minutes. During this operation, pungent vapours are evolved, and with some practice the end of the reaction may be readily detected by the appearance of the melt, which becomes granular and nearly solid. The product, which is coloured dark reddish-brown by the ferric oxide which it contains, is dissolved out by hot water, and transferred to a large porcelain pot ; and when about 2 kilos. of sulphocamphylic acid have been fused in this way, the liquid is acidified and allowed to stand overnight, when the oil which separates will have become semi-solid.

* A description of these interesting acids is reserved for a future communication.

This dark-brown, semi-solid mass is collected, washed with water, and stirred up with ether in large beakers until the organic matter is entirely dissolved; the ethereal solution is then decanted, filtered from the ferric oxide, dried over calcium chloride, and the ether distilled off. The oily residue, which usually weighs about 350 grams, is next twice fractionated under reduced pressure, when nearly the whole passes over between 170—190° (60 mm.) as a pale greenish oil, which on cooling solidifies completely. The crystalline cake is broken up and digested with excess of sodium carbonate and some animal charcoal, filtered, the filtrate acidified, and the crystalline precipitate collected and washed. In this way, a small quantity of a neutral substance smelling strongly of peppermint, and much colouring matter, is removed. In order to purify the crude isolauronolic acid thus obtained, it is dissolved in excess of ammonia, and submitted to distillation in steam, when the ammonium salt of isolauronolic acid dissociates, causing the acid to separate out in the flask, and to be partially carried over with the steam and ammonia. The distillate is acidified, and the precipitate, together with the acid which has separated in the flask, is collected, dissolved in sodium carbonate, heated on the water bath with purified animal charcoal for half an hour, and, after filtering, the acid is re-precipitated and purified by recrystallisation from dilute acetic acid or dilute alcohol, until the melting point rises to 133—135°. The analysis of three different preparations gave the following results.

0·1485 gave 0·3792 CO_2 and 0·1206 H_2O. C = 69·61; H = 9·02.
0·1500 „ 0·3865 CO_2 „ 0·1235 H_2O. C = 70·27; H = 9·28.
0·1489 „ 0·3826 CO_2 „ 0·1218 H_2O. C = 70·05; H = 9·08.

$C_8H_{13}.COOH$ requires C = 70·13; H = 9·09 per cent.

In preparing isolauronolic acid by this method, a quantity of oily impurity is removed from the crude crystals during the crystallisation from dilute acetic acid, and in order to investigate the nature of this, the mother liquors from a very large number of different preparations were mixed with water and extracted with ether. The ethereal solution was several times washed with water to remove the acetic acid, dried over calcium chloride, and evaporated; in this way, about 50 grams of a thick, yellow oil was obtained, which was carefully fractionated, first under reduced pressure, and then under ordinary pressure.

Rather more than 30 grams of the oil distilled between 230° and 245° (750 mm.), and this, on standing for some months in an ice chest, deposited a few crystals of isolauronolic acid. The oil was decanted from these crystals and again distilled, when nearly the whole passed over at 230—235° as a colourless oil, which on analysis gave the following results.

0·1436 gave 0·3548 CO_2 and 0·1236 H_2O. C = 67·45; H = 9·63.
0·1584 „ 0·3905 CO_2 „ 0·1391 H_2O. C = 67·23; H = 9·75.
$C_7H_{13}\cdot COOH$ requires C = 67·60; H = 9·86 per cent.

The silver salt of this acid was prepared by precipitating a slightly alkaline solution of the ammonium salt with silver nitrate; and the white, caseous precipitate was analysed, with the following results.

0·1943 gave 0·2693 CO_2, 0·0860 H_2O, and 0·0855 Ag.
C = 37·80; H = 4·91; Ag = 44·00.
$C_7H_{13}\cdot COOAg$ requires C = 38·55; H = 5·22; Ag = 43·38 per cent.

From these results, it seems probable that this oil, boiling at 230—235°, is an acid of the composition $C_7H_{13}\cdot COOH$, but, as its examination did not give any results which seemed likely to be of value in the present inquiry, its systematic investigation was not undertaken.

Properties and Salts of Isolauronolic Acid.—Isolauronolic acid melts at 133—135°, and distils without decomposition at about 250° under the ordinary pressure; it is readily volatile in steam. It dissolves readily in alcohol, ether, chloroform, benzene, carbon bisulphide or ethylic acetate, but is only very sparingly soluble in water. The solution of the acid in sodium carbonate is oxidised by potassium permanganate instantly at the ordinary temperature, but bromine is not decolorised by the solution of the acid in chloroform except on warming or long standing, and then with evolution of hydrogen bromide. Isolauronolic acid is not readily attacked by hydrogen bromide, since it does not form an additive compound when its solution in glacial acetic acid is saturated with hydrogen bromide and allowed to stand overnight; this is shown to be the case by adding water to the solution, when the acid is reprecipitated unchanged.

Noyes (*Ber.*, 1895, **28**, 552) succeeded in obtaining a dibromide of isolauronolic acid, $C_8H_{13}Br_2\cdot COOH$, melting at 138—140°, by treating the solution of the acid in dry chloroform with bromine, in the dark, at temperatures below 0°, and he has also prepared a crystalline hydrobromide, $C_8H_{14}Br\cdot COOH$ (m. p. 127—130°), which he obtained by shaking the acid with fuming aqueous hydrobromic acid and light petroleum.* Isolauronolic acid is not reduced when treated with a large excess of sodium amalgam, but it yields a *dihydro-derivative*, $C_8H_{15}\cdot COOH$, when its solution in amylic alcohol is heated with sodium (see p. 836).

Isolauronolic acid does not form a lactone when boiled with dilute acids. This point has been very carefully investigated by heating

* Private communication.

the acid with sulphuric acid of varying concentration and under various conditions, but in no case could a lactone be isolated.

The dissociation constant of isolauronolic acid has been determined by Walker (Trans., 1893, **63**, 505) who found the very low value $k = 0{\cdot}0018$.

Isolauronolic acid dissolves in dilute ammonia and in sodium hydrogen carbonate, but it is a very feeble acid, since its ammonium salt readily dissociates into ammonia and the free acid on evaporating its solution on the water bath. Koenigs and Hoerlin (*Ber.*, 1893, **26**, 814) state that the solution of the calcium salt of the acid is decomposed by carbon dioxide into calcium carbonate and the free acid, a decomposition seldom met with in organic calcium salts.

Silver isolauronolate, $C_8H_{13}\cdot COOAg$, was obtained, on adding silver nitrate to a neutral solution of the ammonium salt, as a white, caseous, and very voluminous precipitate which on analysis gave the following results.

I. 0·1967 gave 0·2976 CO_2, 0·0884 H_2O, and 0·0815 Ag.
C = 41·26; H = 4·99; Ag = 41·43.

II. 0·1625 gave 0·0672 Ag. Ag = 41·35.

$C_8H_{13}\cdot COOAg$ requires C = 41·38; H = 4·98; Ag = 41·38.

A neutral dilute solution of the ammonium salt of isolauronolic acid gives, with *copper sulphate*, a light blue, apparently crystalline, and very insoluble precipitate, and with *lead acetate* or *zinc sulphate*, a white, amorphous, caseous precipitate, but no precipitation with *barium* or *calcium chlorides*.

Koenigs and Hoerlin (*loc. cit.*) have prepared and analysed a *calcium salt* of isolauronolic acid, $(C_9H_{13}O_2)_2Ca + H_2O$ (?),* and the *potassium salt*, $C_9H_{13}KO_2 + H_2O$; both of these salts are crystalline and soluble in water; according to Noyes (*Ber.*, 1895, **28**, 550), the calcium salt of isolauronolic acid crystallises with $3\frac{1}{2}H_2O$.

Walker (this Journal, 1893, **63**, 506) has described the *barium salt* of isolauronolic acid as a soluble, crystalline substance, which appears to have the formula $(C_9H_{13}O_2)_2Ba + 5H_2O$.

Ethereal Salts of Isolauronolic Acid.—The methylic and ethylic salts of isolauronolic acid were prepared by dissolving the acid in the corresponding alcohol, adding concentrated sulphuric acid, allowing the mixture to stand for 12 hours, and then heating for 2 hours at 60—80° etherification taking place very readily under these conditions. After adding water, the oily ethereal salts were extracted three times with ether, the ethereal solutions were well washed with water and dilute

* The formula, $C_9H_{13}CaO_2 + H_2O$, given for this salt in Koenigs and Hoerlin's paper is obviously a slip.

sodium carbonate, dried over anhydrous potassium carbonate, and after distilling off the ether, the residue was purified by fractionation under the ordinary pressure. The determination of the densities, magnetic rotation, refraction, &c., of these ethereal salts was carried out by W. H. Perkin, sen.

Methylic isolauronolate, $C_8H_{13}\cdot COOCH_3$, a colourless liquid possessing a rather characteristic odour, boils at 204—204·5° without decomposition.

0·1114 gave 0·291 CO_2 and 0·0962 H_2O. C = 71·24; H = 9·60.
$C_8H_{13}\cdot COOCH_3$ requires C = 71·43; H = 9·52 per cent.

The density determinations gave

d 4°/4° = 0·9835. d 15°/15° = 0·9747.
d 10°/10° = 0·9784. d 25°/25° = 0·9681.

Prepared in the way described above, this methylic salt has a slight permanent rotation, which was found to be + 7′ 48″ for a length of 10·2 cm. at 30°.

	t.	Sp. rotation.	Mol. rotation.
Magnetic rotation	30°	1·1696	11·312
Refraction	t = 17·3°.	d 17·3°/4° = 0·97207.	

	μ.	$\frac{\mu-1}{d}$.	$\frac{\mu-1}{d}p$.
A.....	1·46278	0·47607	79·981
Li	1·46575	0·47913	80·494
Hα	1·46634	0·47974	80·596
Na	1·46970	0·48319	81·176
Hβ	1·47795	0·49168	82·603
Hγ	1·48517	0·49911	83·851

Ethylic isolauronolate, $C_8H_{13}\cdot COOC_2H_5$. B. p. 216°.

0·1170 gave 0·3112 CO_2 and 0·1049 H_2O. C = 72·60; H = 9·96.
$C_8H_{13}\cdot COOC_2H_5$ requires C = 72·53; H = 9·89 per cent.

The density determinations gave

d 4°/4° = 0·9645. d 10°/10° = 0·9596. d 15°/15° = 0·9560.
d 20°/20° = 0·9527. d 25°/25° = 0·9494.

This ethereal salt had a slight permanent rotation which was found to be + 10′ 12″ for a length of 10·2 cm. at 29°.

	t.	Sp. rotation.	Mol. rotation.
Magnetic rotation.....	28·5°	1·1623	12·405
Refraction	t = 17·2°	d 17·2°/4° = 0·95339.	

	μ.	$\frac{\mu-1}{d}$.	$\frac{\mu-1}{d}p$.
A	1·45950	0·48197	87·718
Li	1·46238	0·48498	88·267
Hα ...	1·46307	0·48571	88·400
Na.....	1·46624	0·48903	89·004
Hβ ...	1·47429	0·49748	90·541
Hγ ...	1·48127	0·50478	91·870

The results obtained in the examination of the magnetic rotation of methylic and ethylic isolauronolates are interesting. The difference in the values of the two ethereal salts is 1·093 and is normal, that is to say, it is the same as between the ethylic and methylic salts in the fatty series; thus, for example, the difference between the ethylic and methylic salts of butyric acid is 1·090.

Again, the values obtained afford important evidence that isolauronolic acid is an unsaturated acid, as the following comparison of ethylic isolauronolate with ethylic nonate shows. The magnetic rotation of ethylic nonate, $C_8H_{17}\cdot COOC_2H_5$, is 11·590, and assuming that ethylic isolauronolate is unsaturated, and at the same time a closed chain compound, its magnetic rotation may be approximately calculated.

From the examination of a large number of closed chain compounds, it has been found that these differ from the corresponding open chain saturated compounds by about $-0{\cdot}47$, and also that unsaturated compounds have a higher rotation than the corresponding saturated compounds by about 1·112.

We have, therefore,

Magnetic rotation of ethylic nonate	= 11·590
Add value for unsaturation	= 1·112
	12·702
Deduct value for ring formation	= 0·471
Calculated magnetic rotation of ethylic isolauronolate	= 12·231

The value thus calculated agrees well with that actually found, namely, 12·405.

The refractions of the methylic and ethylic salts of isolauronolic acid are very high, showing their unsaturated nature, as is evident from the following comparison between the values found and those calculated.

	Found.	Calculated.	Difference.
Methylic salt.....	80·596	77·0	+3·504
Ethylic salt	88·400	84·6	+3·800

Methylic dibromisolauronolate, $C_8H_{13}Br_2\cdot COOCH_3$.—The action of

bromine on methylic isolauronolate was investigated in order to obtain further evidence as to the unsaturation of the acid. Methylic isolauronolate (3 grams) was dissolved in carefully dried chloroform (3 grams), and after cooling the solution to 0°, dry bromine (3 grams) dissolved in chloroform (10 grams) was slowly added, the apparatus being covered up so as to exclude light during the operation. The bromine was rapidly, but not instantaneously, absorbed, and as soon as the whole had been decolorised, the product, which, owing to the presence of traces of hydrogen bromide, fumed slightly, was freed from chloroform by passing a current of dry air through it for some hours. The thick oil thus obtained, after standing for some time over solid paraffin wax in a vacuum desiccator, gave the following results on analysis.

0·2171 gave 0·2994 CO_2 and 0·0931 H_2O. C = 37·61; H = 4·76.
0·1899 ,, 0·2536 CO_2 ,, 0·0772 H_2O. C = 36·40; H = 4·50.
0·3329 ,, 0·3696 AgBr; Br = 47·24.
0·4172 ,, 0·4650 AgBr; Br = 47·42.
$C_8H_{13}Br_2 \cdot COOCH_3$ requires C = 36·6; H = 4·87; Br = 48·77.

These results show that very little hydrogen bromide is eliminated when methylic isolauronolate is treated with the calculated quantity of bromine at 0° in the dark, since the product contains almost the quantity of bromine theoretically required for the dibrom-additive compound.

Conversion of Isolauronolic Acid into Sulphocamphylic Acid.

When isolauronolic acid, in quantities of 0·5 gram, is added to 10 times its weight of concentrated sulphuric acid, it dissolves with development of some heat, and formation of a yellow solution from which water precipitates the acid unchanged. If, however, the solution is gradually heated to 75°, it darkens and becomes brownish-black, a small amount of sulphur dioxide is liberated, and after heating some time no isolauronolic acid is deposited on adding water. After about 20 minutes heating at 75°, and as soon as a drop of the solution gave no precipitate on diluting with water, the well-cooled product was gradually mixed with an equal bulk of water, and the greenish solution left for some hours, when crystals separated; these were collected with the aid of the pump, dissolved in a little water, the solution warmed with animal charcoal, filtered, and evaporated nearly to dryness on the water bath. On standing in the ice chest, beautiful crystals of sulphocamphylic acid gradually formed; after draining these on a porous plate and subsequently drying at 130°, they gave the following results on analysis.

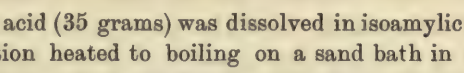
0·5547 gave 0·5451 $BaSO_4$. S = 13·43.

$C_8H_{12}(SO_3H)\cdot COOH$ requires S = 13·68 per cent.

The careful examination of the properties of these crystals proved conclusively that they consisted of sulphocamphylic acid, and this acid, which is produced almost quantitatively in this way, is evidently formed from isolauronolic acid by the addition of sulphuric acid and elimination of water thus.

$$C_8H_{13}\cdot COOH + H_2SO_4 = C_8H_{12}(SO_3H)\cdot COOH + H_2O.$$

Dihydroisolauronolic Acid,



In the first experiments on the reduction of isolauronolic acid, it was treated with sodium amalgam under varied conditions, but no reduction took place even when its solution in sodium carbonate was boiled with a large excess of the amalgam; ultimately, it was found that the acid could be reduced, although with difficulty, when its solution in amylic alcohol was treated with sodium at the boiling temperature.

Pure isolauronolic acid (35 grams) was dissolved in isoamylic alcohol ($1\frac{1}{2}$ litres), the solution heated to boiling on a sand bath in a flask connected with a long reflux condenser, and then 10 grams of sodium, in small pieces, was added all at once; as soon as the violent action had moderated somewhat, 20 grams more sodium was added, and the whole boiled vigorously until the sodium had dissolved. After allowing the mixture to cool, water was added, the product acidified with hydrochloric acid, the oily layer separated, and the aqueous liquid extracted twice with small quantities of isoamylic alcohol. The extract was then added to the main bulk, the whole distilled until the thermometer rose to 125°, when it was treated again with 30 grams of sodium exactly as in the first instance. After this process had been repeated three times, the product was extracted with water three times, the isoamylic alcohol distilled down to a small bulk, the remainder removed by distillation with steam, and the aqueous solution thus obtained added to the previous extracts. The whole was then heated on the water bath until quite free from isoamylic alcohol, acidified, and repeatedly extracted with ether; after drying over calcium chloride and evaporating off the ether, 35 grams of an almost colourless oil was obtained which, on standing for some days in an ice chest, deposited about 5 grams of unchanged isolauronolic acid. These crystals were removed by filtration, and the filtrate distilled; almost

the whole passed over at 165° (at 30 mm.) as a colourless oil which gave the following results on analysis.

0·1292 gave 0·3284 CO_2 and 0·1163 H_2O. C = 69·27 ; H = 10·00.
C_8H_{15}·COOH requires C = 69·23 ; H = 10·25 per cent.

Although this analysis agrees well with the numbers required by dihydroisolauronolic acid, it was found that when a drop of the substance dissolved in dilute sodium carbonate was mixed with a trace of permanganate, the colour was instantly discharged, showing that it still contained some unchanged isolauronolic acid, and since, for subsequent experiments, it was necessary that this should be removed, the following process of purification was resorted to.

The acid was dissolved in dilute sodium carbonate and oxidised by dilute permanganate in a vessel fitted with a turbine, the temperature being kept at 0° by means of powdered ice, and a rapid current of carbonic anhydride being passed during the whole operation. As soon as the pink colour remained permanent for several minutes, the excess of permanganate was destroyed by sodium hydrogen sulphite, the whole heated to boiling, filtered, and the filtrate and washings from the manganese precipitate evaporated to dryness. The residue was acidified, distilled in a current of steam,* the oily acid extracted from the distillate in the usual way, and purified by distillation under reduced pressure, when nearly the whole passed over at 144° (22 mm.).

0·1272 gave 0·3221 CO_2 and 0·1168 H_2O. C = 69·04 ; H = 10·22.
C_8H_{15}·COOH requires C = 69·23 ; H = 10·25 per cent.

Dihydroisolauronolic acid is a colourless, moderately mobile oil which smells like a high boiling fatty acid. It dissolves readily in sodium carbonate, and the solution of the sodium salt does not decolorise permanganate in the cold. The acid is, in fact, characterised by extraordinary stability, as even when boiled with permanganate it is only very slowly attacked, and all attempts to oxidise it with nitric acid were unsuccessful, since, after boiling it for a week with 50 per cent. nitric acid, more than 75 per cent. of the acid was recovered unchanged.

Salts of Dihydroisolauronolic Acid.—The *silver salt*, C_8H_{15}·COOAg, obtained as a white, gelatinous precipitate by adding silver nitrate to a slightly alkaline solution of the ammonium salt, was washed well with water and once with methylic alcohol.

0·2338 gave 0·0950 Ag. Ag = 40·64.
$C_8H_{15}COOAg$ requires Ag = 41·06 per cent.

* A considerable quantity of isolauronic acid separated from the residue in the distilling flask on standing.

This salt is very sparingly soluble in water, but it dissolves moderately readily in alcohol.

The *ammonium salt*, which separates in colourless crystals when the acid is mixed with moderately concentrated ammonia, is readily soluble in water, and dissociates when its solution is evaporated on the water bath. A slightly alkaline solution of the ammonium salt shows the following behaviour with reagents.

Barium chloride, no precipitate in the cold, but on boiling a crystalline barium salt separates, the crystals dissolving again on cooling.

Calcium chloride gives no precipitate with dilute solutions, but with moderately concentrated solutions a white calcium salt separates as an amorphous mass which becomes crystalline on warming.

Copper acetate gives at once a very pale blue, amorphous precipitate.

Bromination of Dihydroisolauronolic Acid, and its Reconversion into Isolauronolic Acid.

This experiment, which has such an important bearing on the constitution of isolauronolic acid (p. 810), was conducted as follows.

Dihydroisolauronolic acid (3 grams) was mixed in a reflux apparatus with phosphorus pentabromide (8 grams), and after the reaction, which commenced at once, had ceased, the mixture was heated for 10 minutes on the water bath. Bromine (3 grams) was then added to the well cooled product, and the whole very gently heated until the evolution of hydrogen bromide had practically ceased, and the colour of the bromine had disappeared.

The mixture of bromacid bromide and phosphorus oxybromide thus obtained was poured in a thin stream into excess of methylic alcohol; water was added, and the methylic salt, extracted with ether in the usual way, was washed with dilute sodium carbonate, dried, and fractionated under reduced pressure. Almost the whole of it (6 grams) distilled at 123—126° (30 mm.) as a colourless oil, and with liberation of traces of hydrogen bromide, which accounts for the analytical results being a little low.

0·3134 gave 0·2230 AgBr. Br = 30·27.
0·2904 „ 0·2050 AgBr. Br = 30·03.
$C_8H_{14}Br\cdot COOCH_3$ requires Br = 32·12 per cent.

When this *methylic bromodihydroisolauronolate* * is mixed with warm alcoholic potash, a vigorous action takes place, accompanied by separation of potassium bromide, and if, after boiling for some minutes,

* The free acid, called by Noyes α-bromodihydro-*cis*-campholytic acid, is crystalline and melts at 124–125° (*Journ. Amer. Chem. Soc.*, 1896, **18**, 689).

water is added and the alcohol removed by evaporation, a residue is obtained which, on acidifying, gives a crystalline precipitate; this, after being freed from traces of oily impurity by spreading it on porous porcelain, crystallises beautifully from dilute alcohol, and consists of pure isolauronolic acid (m. p. 133°).

0·1474 gave 0·1205 H_2O and 0·3793 CO_2. C = 70·18; H = 9·08.
$C_8H_{13}\cdot COOH$ requires C = 70·13; H = 9·09 per cent.

The yield of isolauronolic acid obtained in this way appears to be almost quantitative.

Isolauronic Acid, $(CH_3)_2C$(CH$_2$—C·COOH)$\cdot$CH$_3$·C—CO

This acid was first described by Koenigs and Meyer (*Ber.*, 1894, **27**, 3467), who obtained it by oxidising isolauronolic acid with potassium permanganate at 0°.

Almost at the same time, and quite independently, the author carried out a series of experiments on the oxidation of isolauronolic acid, and after preparing a quantity of isolauronic acid, carefully investigated it, with the result that many fresh facts were discovered which throw important light on the constitution both of this acid and of isolauronolic acid.

The isolauronic acid used in these experiments was prepared as follows. Pure isolauronolic acid (5 grams) was dissolved in a slight excess of warm dilute potash, the solution transferred to a large porcelain beaker fitted with a turbine, and a rapid stream of carbon dioxide passed through the liquid. After adding powdered ice, and cooling the beaker externally by a freezing mixture, so that the temperature of the solution never exceeded −3°, a well cooled saturated solution of potassium permanganate was slowly run in until the colour, which at first instantly disappeared, just remained permanent, the whole being stirred continuously, and a rapid current of carbon dioxide passed during the operation.*

After the excess of permanganate had been destroyed by adding a little sodium hydrogen sulphite, the product was heated on the water bath, filtered from the manganese precipitate, and the filtrate, together with the washings of the precipitate, evaporated to a small bulk. On acidifying the deep yellow solution thus obtained, it deposited a mass of yellow crystals of isolauronic acid,† which were collected with

* If these precautions are not taken, the yield of isolauronic acid is very much reduced.

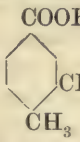
† The mother liquors from these crystals contain considerable quantities of γ-dimethylacetylbutyric acid (see p. 844).

the aid of the pump, washed with water, and purified by recrystallisation from this solvent.

0·1730 gave 0·4069 CO_2 and 0·1141 H_2O. C = 64·16 ; H = 7·32.
0·1557 „ 0·3667 CO_2 „ 0·1029 H_2O. C = 64·22 ; H = 7·34.
$C_9H_{12}O_3$ requires C = 64·22 ; H = 7·14 per cent.

Isolauronic acid crystallises from water in long, glistening, straw-yellow prisms and melts at 133°. It is readily soluble in hot water, ether, and alcohol, but only sparingly in light petroleum and cold water ; it dissolves readily in sodium carbonate, and although the solution does not decolorise permanganate below 0°, it does so readily at the ordinary temperature. Isolauronic acid does not appear to form an additive compound with hydrogen bromide, since the solution of the acid in acetic acid saturated with hydrogen bromide, even on long standing, gives a precipitate of the unchanged acid on the addition of water. A solution of bromine in caustic potash oxidises the acid particularly easily on warming, with separation of bromoform and formation of an oily acid, which is at present under investigation.

Bromine vapour converts isolauronic acid into a red liquid, which gradually solidifies on standing over potash in a vacuum ; the crystals, however, are very deliquescent, and as the substance could not be purified by recrystallisation from solvents, it was not further investigated.

When heated with concentrated aqueous hydrochloric acid at 170° for 3 hours, isolauronic acid is completely changed, with separation of a certain amount of carbonaceous matter. In order to find out what had been formed during this decomposition, the product was extracted with ether, the ethereal extract evaporated, the solid residue dissolved in sodium carbonate, and the solution, after boiling with animal charcoal and filtering, evaporated to a small bulk and acidified with hydrochloric acid. The almost colourless, sparingly soluble, sandy precipitate, which melted at 165°, after crystallisation from acetic acid, was, on investigation, found to be paraxylic acid,  , an acid which Koenigs and Meyer (*Ber.*, 1894, 27, 3468) had already obtained from isolauronic acid by treatment with sulphuric acid.

Salts of Isolauronic Acid.—The *silver salt*, $C_9H_{11}AgO_3$, is obtained by adding silver nitrate to a warm neutral solution of the ammonium salt, as a colourless, crystalline precipitate, which dissolves moderately readily in hot water, and separates again on cooling as a beautiful, silky mass of crystals.

0·1732 gave 0·2492 CO_2, 0·0642 H_2O and 0·0684 Ag.
C = 39·24 ; H = 4·12 ; Ag = 39·48.
$C_9H_{11}AgO_3$ requires C = 39·27 ; H = 4·00 ; Ag = 39·27 per cent.

A dilute neutral solution of the ammonium salt of isolauronic acid gives no precipitate with *barium* or *calcium* chlorides even on boiling ; the addition of *copper* sulphate produces no precipitate in the cold, but on boiling a very pale blue, apparently crystalline, salt separates ; *lead* acetate gives at once a white, caseous precipitate which is soluble in hot water.

Oxime of Isolauronic Acid, $C_7H_{11}(C{:}NOH)\cdot COOH$.—The action of hydroxylamine on isolauronic acid has been studied by Carl Meyer (*Dissertation Munich*, 1895, p. 39), who obtained in this way the oxime which he describes as a pale yellow powder which softens at 215° and decomposes at 228—230°. In preparing this substance in considerable quantities for experiments in connection with this research, the following method was always used. The pure acid (5 grams) was dissolved in moderately strong potash (15 grams), a solution of hydroxylamine hydrochloride (7 grams) added, and the whole after standing overnight was acidified, when the oxime was precipitated as a voluminous, amorphous precipitate somewhat resembling a precipitate of alumina. The whole was extracted 20 times with ether, and the ethereal solution, after being rapidly dried over calcium chloride, was evaporated until crystalline crusts of the oxime commenced to separate. After standing for some time, these were collected, washed with ether, and analysed.

0·1240 gave 8 c.c. of nitrogen at 18° and 762 mm. N = 7·47.
$C_9H_{13}NO_3$ requires N = 7·65 per cent.

When heated in a capillary tube, the oxime of isolauronic acid turns brown at 210°, and melts with vigorous decomposition at 222°.

Semicarbazone of Isolauronic Acid, $C_7H_{11}(C{:}N_2H\cdot CO\cdot NH_2)\cdot COOH$.—This very characteristic derivative is readily prepared by warming isolauronic acid with a slight excess of semicarbazide hydrochloride and sodium acetate on the water bath for a few minutes. The very sparingly soluble precipitate which separates rapidly on cooling was collected, washed with water, recrystallised from alcohol, and analysed, with the following result.*

0·1444 gave 23·9 c.c. nitrogen at 20° and 740 mm. N = 18·42.
0·2178 „ 36·1 c.c. „ 18° „ 745 mm. N = 18·70.
$C_{10}H_{15}N_3O_3$ requires N = 18·66 per cent.

* Carl Meyer (*Dissertation Munich*, 1895, p. 39), who has also prepared this semicarbazone, states that he always found 1 per cent. too much nitrogen in his analyses.

The *semicarbazone* of isolauronic acid melts at about 247—248° with decomposition.

Oxidation of Isolauronic Acid. Formation of γ-Dimethylacetylbutyric Acid, $CH_3 \cdot CO \cdot C(CH_3)_2 \cdot CH_2 \cdot CH_2 \cdot COOH$, *and α-Dimethylsuccinic Acid,* $COOH \cdot C(CH_3)_2 \cdot CH_2 \cdot COOH$.

I. *α-Dimethylsuccinic Acid.*—In the first experiments on the oxidation of isolauronic acid, 3 grams of the pure acid were dissolved in hot water, the solution heated to boiling in a reflux apparatus and then potassium dichromate and sulphuric acid run in through a tap funnel until very little further oxidation appeared to take place. The green solution, after saturating with ammonium sulphate, was extracted 10 times with ether, and the ethereal solution dried over calcium chloride and evaporated, when nearly 2 grams of a thick oil were obtained, which deposited crystals on standing; these were collected, drained on a porous plate, recrystallised from concentrated hydrochloric acid, and analysed, with the following result.

0·1520 gave 0·274 CO_2 and 0·0958 H_2O. C = 49·15; H = 7·0.
$C_6H_{10}O_4$ requires C = 49·31; H = 6·85 per cent.

This substance melted at 138—140°, and it seemed probable that it was identical with the α-dimethylsuccinic acid,

$$COOH \cdot C(CH_3) \cdot CH_2 \cdot COOH,$$

which Leuckart (*Ber.*, 1885, **18**, 2250) and Bischoff and Jaunsnicker (*Ber.*, 1890, **23**, 3400) had obtained by the hydrolysis of the product of the action of ethylic α-bromoisobutyrate on the sodium compound of ethylic malonate. In order to decide this point, the acid obtained from isolauronic acid was carefully compared with a sample of the synthetical acid which Professor Bischoff kindly sent the author, and in this way the identity of the two acids was clearly proved.

As it is a matter of importance, particularly for those working in the camphor group, to be able quickly to identify small quantities of α-dimethylsuccinic acid, a short account of the more characteristic properties of this acid, together with a description of some new derivatives which were prepared during the above experiments, is given here.

α-Dimethylsuccinic acid is best purified by dissolving it in a little water, and saturating the well cooled solution with hydrogen chloride; on cooling, the acid rapidly separates in small crystals, which, after collecting on an asbestos filter, washing with hydrochloric acid, and draining on a porous plate, melt at 138—140°.

A characteristic of dimethylsuccinic acid, which is often very valuable in separating the acid from a mixture with other acids, is

the property that, when its aqueous solution is made strongly alkaline with ammonia and then mixed with excess of calcium chloride solution, no precipitate is formed in the cold, but on boiling a very sparingly soluble calcium salt separates, which, after collecting, washing with water, decomposing with hydrochloric acid and extracting with ether, yields at once the pure acid.*

α-Dimethylsuccinanilic acid is readily prepared by heating the acid with excess of acetyl chloride for a few minutes, and after evaporating the excess of the chloride, dissolving the residue in benzene and adding aniline. In a short time, the anilic acid separates in crystals, which, after collecting and purifying by recrystallisation from dilute methylic alcohol, melt, when rapidly heated, at about 187° with rapid decomposition. The following analyses were made.

I. (From isolauronic acid) 0·1796 gave 9·8 c.c. of nitrogen at 16° and 755 mm. N = 6·32.

II. (From synthetical acid) 0·2695 gave 14·8 c.c. of nitrogen at 15° and 752 mm. N = 6·36.

$C_{12}H_{15}NO_3$ requires N = 6·33 per cent.

This anilic acid is readily decomposed by heating at 200—210°, with elimination of water and formation of *α-dimethylsuccinanil*,

$$\begin{array}{l} CO\cdot C(CH_3)_2\cdot CH_2\cdot CO, \\ \quad\backslash\!\!-\!\!-N(C_6H_5)-\!\!-\!\!/ \end{array}$$

a colourless, crystalline substance which, after recrystallisation from light petroleum (boiling point, 80—100°), melts at 87°. The following analyses were made.

I. (From isolauronic acid) 0·1801 gave 10·6 c.c. of nitrogen at 17° and 756 mm. N = 6·80.

II. (From synthetical acid) 0·2420 gave 14·9 c.c. of nitrogen at 15° and 760 mm. N = 7·21.

$C_{12}H_{13}NO_2$ requires N = 6·89 per cent.

* This property has been made use of with great success in preparing α-dimethylsuccinic acid from the product of the action of ethylic α-bromisobutyrate on the sodium compound of ethylic malonate. When the product of this reaction is hydrolysed, a mixture of α-dimethylsuccinic acid and α-methylglutaric acid, $COOH\cdot CH(CH_3)\cdot CH_2\cdot CH_2\cdot COOH$, is obtained, and these two acids can only be separated with difficulty by crystallisation. If, however, the mixed acids are dissolved in excess of ammonia, calcium chloride added, and the clear solution heated to boiling, the whole of the calcium dimethylsuccinate is precipitated, whereas the calcium salt of methylglutaric acid remains in solution.

II. *γ-Dimethylacetylbutyric Acid*, $CH_3 \cdot CO \cdot C(CH_3)_2 \cdot CH_2 \cdot CH_2 \cdot COOH$.

In oxidising isolauronic acid in the way just described, it was observed that the mother liquors from which the crude dimethylsuccinic acid had separated, and from which the last traces of this acid had been removed by calcium chloride, contained an oily acid which gave a precipitate of bromoform on treatment with bromine and caustic potash. In order to find out what this acid was, the oxidation was repeated under various conditions, but without result until ultimately the following process was devised.

Isolauronic acid (10 grams), in quantities of 1 gram, was oxidised on the water bath by means of potassium dichromate and sulphuric acid in such a way that, on cooling the solution, a small quantity of unchanged isolauronic acid always separated.* The product from the 10 oxidations was left in an ice chest overnight, filtered from the long crystals of isolauronic acid which separated, the green solution evaporated at 50° to a small bulk, and extracted 10 times with pure ether. On evaporating the ether, a dark brown oil was obtained, which, although it was readily soluble in water, contained besides dimethylsuccinic acid and the new ketonic acid, also appreciable quantities of isolauronic acid. The whole was dissolved in a slight excess of ammonia, boiled with calcium chloride to precipitate the calcium dimethylsuccinate, filtered, acidified, and again repeatedly extracted with ether; after drying over calcium chloride, the ether was distilled off, and a light yellow, oily residue was left, which, even after standing for some weeks, did not show any signs of crystallising.

The crude oil was dissolved in water, mixed with a large excess of semicarbazide hydrochloride and the corresponding quantity of sodium acetate, and heated on a water bath at 60° for about 15 minutes, when a brownish semicarbazide rapidly separated, and on standing overnight a further quantity of a much paler coloured, crystalline precipitate was deposited. The whole was collected, washed with water, and boiled with a large quantity of water; about half the semicarbazide dissolved,† and on filtering while hot and allowing the filtrate to stand for some days, a brown, sandy precipitate gradually crystallised out. This was collected, purified by recrystallisation from large quantities of alcohol, and the colourless, crystalline precipitate thus obtained analysed, with the following results.

* The isolauronic acid recovered from these oxidations crystallised from water in beautifully glistening needles which were nearly colourless, whereas this acid prepared as described in this paper, is always obtained in straw-yellow crystals; the yellow colour is therefore obviously due to impurity.

† The portion which remained undissolved was found on examination to consist of the semicarbazide of isolauronic acid.

0·1381 gave 0·2537 CO_2 and 0·0974 H_2O. C = 50·07; H = 7·83.
0·1314 „ 22·4 c.c. nitrogen at 17° and 758 mm. N = 19·72.
$C_9H_{17}N_3O_3$ requires C = 50·24; H = 7·9; N = 19·53 per cent.

The subsequent examination showed that this was the *semicarbazide* of γ-acetyldimethylbutyric acid,

$$CH_3 \cdot C(N_2H \cdot CO \cdot NH_2) \cdot C(CH_3)_2 \cdot CH_2 \cdot CH_2 \cdot COOH.$$

γ-Acetyldimethylbutyric acid was obtained from the semicarbazide by heating it on the water bath with dilute hydrochloric acid (1 vol. HCl to 2 vols. H_2O) until the crystals had entirely dissolved, and then extracting the liquid repeatedly with pure ether. The ethereal solution, when dried over calcium chloride and evaporated, deposited a nearly colourless oil, which solidified when left over sulphuric acid for some days; on leaving the crystalline mass in contact with porous plates, the traces of oily impurity were completely absorbed, and colourless crystals were left, which, on analysis, gave the following results.

0·1572 gave 0·3487 CO_2 and 0·1236 H_2O. C = 60·49; H = 8·73.
0·1415 „ 0·3145 CO_2 „ 0·1126 H_2O. C = 60·62; H = 8·83.
$CH_3 \cdot CO \cdot C(CH_3)_2 \cdot CH_2 \cdot CH_2 \cdot COOH$ requires C = 60·76; H = 8·86.

γ-Acetyldimethylbutyric acid melts at about 50—51°, and is so readily soluble in organic solvents that it could not be satisfactorily recrystallised. This acid is identical with dimethyl-3-hexanon-2 acid, which Tiemann (*Ber.*, 1895, **28**, 2176) prepared by the oxidation of β-dihydroxydihydrocampholenic acid with chromic acid mixture, and the melting point of which he found to be 48—49°.

Oxime of γ-Acetyldimethylbutyric Acid,

$$CH_3 \cdot C(NOH) \cdot C(CH_3)_2 \cdot CH_2 \cdot CH_2 \cdot COOH.$$

—In order to prepare this derivative, the acid (3 grams) was dissolved in dilute potash (4 grams), a strong solution of hydroxylamine hydrochloride (3 grams) added, and the whole allowed to stand overnight; on acidifying, a viscid mass separated, which, on shaking, rapidly solidified; this was collected, dried on a porous plate, purified by recrystallisation from hot water, and analysed.

0·1556 gave 0·3196 CO_2 and 0·1242 H_2O. C = 56·01; H = 8·87.
0·2432 „ 18 c.c. of nitrogen at 20° and 760 mm. N = 8·46.
$C_8H_{15}NO_3$ requires C = 55·49; H = 8·67; N = 8·09 per cent.

This oxime is readily soluble in hot water, sparingly in cold water, and crystallises in long, colourless needles which melt at 97—98°.

Reduction of γ-Acetyldimethylbutyric Acid. Formation of the Lactone of γ-Dimethyl-δ-hydroxycapronic Acid, $CH_3\cdot\underset{\displaystyle O}{\underset{|}{C}}H\cdot C(CH_3)_2\cdot CH_2\cdot\underset{\displaystyle CO}{\underset{|}{C}}H_2$.

The reduction of acetyldimethylbutyric acid was investigated, as it was thought possible that the hydroxy-acid formed might be of value in connection with some synthetical experiments which are being carried out in the camphor series.

About 15 grams of the acid was dissolved in dilute sodium carbonate, and treated at the ordinary temperature with 500 grams of 3 per cent. sodium amalgam; after standing overnight, 200 grams more amalgam was added, and the whole heated on the water bath to complete the reduction. The alkaline solution, separated from the mercury, was acidified, saturated with ammonium sulphate, and extracted 10 times with ether; the ethereal solution was then dried with calcium chloride, evaporated, and the oily residue of hydroxy-acid submitted to fractional distillation. During this distillation, much water is eliminated, the thermometer then rises to 235°, almost the whole passing over between 235° and 245°, and, on again distilling, the lactone is easily obtained pure as a colourless oil possessing a faintly camphor-like odour, and boiling at 239—241°.

I. 0·1235 gave 0·3074 CO_2 and 0·1056 H_2O. C = 67·88; H = 9·50.
II. 0·1358 „ 0·3366 CO_2 „ 0·1189 H_2O. C = 67·60; H = 9·72.
$C_8H_{14}O_2$ requires C = 67·60; H = 9·85 per cent.

The *lactone of dimethylhydroxycapronic acid* is isomeric with, and closely related to, the lactone of γ-ethyl-δ-hydroxycapronic acid, $CH_3\cdot\underset{\displaystyle O}{\underset{|}{C}}H\cdot CH(C_2H_5)\cdot CH_2\cdot\underset{\displaystyle CO}{\underset{|}{C}}H_2$, which Fittig and Christ (*Annalen*, 1892, **268**, 122) obtained by the reduction of γ-ethyl-γ-acetylbutyric acid, and which boils at 254—255°.

It is insoluble in water, and dissolves only very slowly on boiling with sodium carbonate solution. Caustic alkalis, however, readily dissolve it, with formation of the salts of the hydroxy-acid.

Oxidation of Acetyldimethylbutyric Acid. Formation of α-Dimethylglutaric Acid, $COOH\cdot C(CH_3)_2\cdot CH_2\cdot CH_2\cdot COOH$.

When treated with bromine and caustic potash, acetyldimethylbutyric acid is readily oxidised, with separation of bromoform or tetrabromomethane, and formation of α-dimethylglutaric acid.

In investigating this decomposition, the pure acetyl acid was dissolved in a large excess of moderately concentrated aqueous potash,

the solution cooled to 0°, and bromine added, until, so far as could be seen, no further deposition of tetrabromomethane took place, and the solution, after standing for some minutes, was found to contain excess of hypobromite. After destroying the excess of hypobromite by passing sulphur dioxide into the solution, it was acidified with hydrochloric acid, saturated with ammonium sulphate, and extracted five times with pure ether; the ethereal solution, dried over calcium chloride, was then evaporated, when an oily residue was left, which, on standing in a vacuum over sulphuric acid, rapidly solidified.* The crystalline mass was dissolved in a little water, and the well cooled solution saturated with hydrogen chloride, when, in a few hours, colourless, needle-shaped crystals separated; these, after draining on a porous plate and drying in a desiccator over potash and sulphuric acid, gave the following results on analysis.

I. 0·1408 gave 0·2701 CO_2 and 0·0956 H_2O. C = 52·32; H = 7·53.
II. 0·1126 „ 0·2168 CO_2 „ 0·0765 H_2O. C = 52·51; H = 7·62.
$COOH\cdot C(CH_3)_2\cdot CH_2\cdot CH_2\cdot COOH$ requires C = 52·50; H = 7·50 per cent.

α-Dimethylglutaric acid melts at about 84°, and is readily soluble in water, alcohol, and most organic solvents, but only very sparingly in cold concentrated hydrochloric acid, separating from its hot solution in this solvent in woolly masses of fine needles. This acid has also been prepared by Tiemann (*Ber.*, 1895, **28**, 2176), who showed that, when oxidised by nitric acid, it yields α-dimethylsuccinic acid, $COOH\cdot C(CH_3)_2\cdot CH_2\cdot COOH$.

α-Dimethylglutaric Anhydride, $\begin{matrix} C(CH_3)_2\cdot CH_2\cdot CH_2 \\ | \qquad\qquad\quad | \\ CO\text{——}O\text{——}CO \end{matrix}$.

This was prepared by digesting the pure acid with excess of acetic anhydride for half an hour, and allowing the solution to evaporate over potash in a vacuum desiccator, when a colourless, syrupy residue was obtained, which soon solidified on being rubbed with a glass rod. The crystalline mass, after draining on a porous plate, melted at 38°, and consisted of α-dimethylglutaric anhydride, as the following analysis shows.

0·1088 gave 2365 CO_2 and 0·0698 H_2O. C = 59·27; H = 7·13.
$C_7H_{10}O_3$ requires C = 59·15; H = 7·04 per cent.

α-Dimethylglutaranilic Acid,
$CO(NH\cdot C_6H_5)\cdot C(CH_3)_2\cdot CH_2\cdot CH_2\cdot COOH$ (?).
—When a solution of dimethylglutaric anhydride in pure benzene is

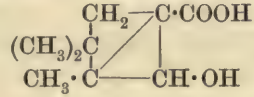
* If the oil does not solidify rapidly, the treatment with potash and bromine must be repeated.

mixed with the calculated quantity of aniline, the corresponding anilic acid rapidly separates in crystals. These were collected, drained on a porous plate, and purified by recrystallisation from dilute alcohol, from which the substance separates in lustrous plates melting at 144° without decomposition.

0·2205 gave 11·5 c.c. of nitrogen at 16·5° and 768 mm. N = 6·07.
$C_{13}H_{17}NO_3$ requires N = 5·96 per cent.

a-Dimethylglutaranilic acid is readily soluble in alcohol, but only sparingly so in water, benzene, or light petroleum.

Reduction of Isolauronic Acid. Formation of Dihydroisolauronic Acid,



The reduction of isolauronic acid was first studied by Carl Meyer (*Dissertation Munich,* 1895, p. 45), who treated the solution of the acid (1 gram) in sodium carbonate at ordinary temperatures with 40—50 grams of 3 per cent. sodium amalgam, a slow current of carbon dioxide being passed during the operation. After 24 hours, he acidified the product, digested it with dilute sulphuric acid for 1 hour, and then extracted with ether; the ethereal solution, after shaking with sodium carbonate to remove an acid (which is mentioned below) and evaporating off the ether, deposited a crystalline lactone, $C_9H_{14}O_2$, which melted at 47—50°, and gave on hydrolysis a hydroxy-acid melting at 143°; it had, in fact, as mentioned in the Introduction, the properties of campholactone. On acidifying the soda solution from which the lactone had been extracted with ether, Carl Meyer obtained an oily acid which gradually solidified; this crystallised from light petroleum in nodular masses, and melted at 80—81°, the melting point not being altered by repeated crystallisation from light petroleum.

The analysis of this substance gave numbers which Carl Meyer thought indicated that it was a mixture of two acids, $C_9H_{14}O_3$ and $C_9H_{16}O_3$.

Found, as a mean of four analyses, C = 62·95; H = 8·66 per cent.
$C_9H_{14}O_3$ requires C = 63·53; H = 8·23 per cent.
$C_9H_{16}O_3$ „ C = 62·71; H = 9·30 „

This acid was not further reduced on treatment with sodium amalgam for several hours on the water bath; and, although no experiment seems to have been made with the object of determining whether it

was capable of forming a lactone, its method of isolation would seem to show that this is not the case.

In assigning the relative positions of the CO and COOH groups in isolauronic acid, it is obvious that it is a matter of the greatest importance to determine whether the acid formed by reducing this ketonic acid is capable of forming a lactone, and, for this reason, a very large number of experiments were instituted on the reduction of isolauronic acid under varied conditions. In the first place, Carl Meyer's experiment was repeated several times exactly as he described it, and using very pure isolauronic acid; but no trace of lactone could be obtained, and the hydroxy-acid, after extraction with ether and evaporating the solvent, solidified at once, and crystallised from light petroleum (b. p. 40—45°) in colourless leaflets which soften at 84—85° and melt at 88—89°.

The analysis gave numbers agreeing sharply with the formula $C_9H_{14}O_3 = C_7H_{11}(CH\cdot OH)\cdot COOH$.

0·1478 gave 0·3429 CO_2 and 0·1090 H_2O. C = 63·27; H = 8·19.
0·1332 ,, 0·3099 CO_2 ,, 0·0985 H_2O. C = 63·45; H = 8·22.
$C_9H_{14}O_3$ requires C = 63·53; H = 8·23 per cent.

This acid, for which the name *dihydroisolauronic acid* is proposed, was formed in all the experiments on the reduction of isolauronic acid, even when very varying conditions of temperature, concentration of solution, and quantities of reagents were employed, and it was the only product of reduction which the author could isolate. Dihydroisolauronic acid is moderately easily soluble in hot water, and crystallises from it, under certain conditions, in beautiful, colourless, glistening, prismatic needles which melt at 88—89°; it is very readily soluble in most organic solvents, and crystallises fairly well from light petroleum.

The solution of dihydroisolauronic acid in dilute sodium carbonate does not decolorise permanganate, except on long standing, and since it does not react with hydrobromic acid at the ordinary temperature, and its solution in chloroform does not decolorise bromine, it appears to be a saturated acid; this is confirmed by the fact, noticed by Carl Meyer, that the acid is not further reduced by sodium amalgam, even at 100°.

Dihydroisolauronic acid dissolves in concentrated sulphuric acid at 30°, forming a yellow solution, and at 40—50° decomposition sets in, with evolution of sulphur dioxide. If, after heating for a few minutes on the boiling water bath, the dark-coloured solution is poured into water, a yellow precipitate separates, which, on recrystallisation from acetic acid, melts at 164—165° and shows all the properties of paraxylic acid.

Attempts to Convert Dihydroisolauronic Acid into a Lactone.

For reasons stated in the Introduction to this paper, it was most important to determine whether dihydroisolauronic acid was capable of forming a lactone, and many experiments were made to decide this point.

I. In three experiments, the pure acid was digested with sulphuric acid of 10, 15, and 20 per cent. for 1 hour. The products from the first two experiments were extracted with ether, and the ethereal solution, after treatment with sodium carbonate, evaporated, but no trace of a lactone was obtained in either case, and on acidifying the sodium carbonate solution, the hydroxy-acid was recovered unchanged.

In the third experiment, in which 20 per cent. sulphuric acid had been used, the solution, on standing overnight, became filled with beautiful, glistening plates which melted at 87° with slight previous softening, and on examination were found to consist of the unchanged hydroxy-acid.

II. Dihydroisolauronic acid was heated in a sealed tube with water at 220° for 3 hours. On opening the tube, there was no pressure, and the light yellow oil which had separated below the water, on being touched with a crystal of the acid, solidified at once, and the crystals, after spreading on a porous plate, melted at 85—87°.

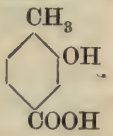
III. When heated in small quantities in a test-tube, dihydroisolauronic acid distils at a high temperature and condenses on the cooler portion of the tube as an oil which rapidly solidifies; the crystals, after being freed from traces of impurity by spreading on a porous plate, melt at 80—85° and consist of the unchanged acid, showing that the hydroxy-acid undergoes very little decomposition when distilled under the ordinary pressure. In order to clearly prove that dihydroisolauronic acid does not yield a lactone on heating, about 5 grams of the carefully dried acid was slowly distilled under reduced pressure (65 mm.); no elimination of water was observed, and the thermometer at once rose to 215°, the whole passing over between this temperature and 220° as a colourless oil which, on touching with a crystal of the original acid, immediately and completely solidified. This distilled acid, without further purification, gave the following results on analysis.

0·1771 gave 0·4152 CO_2 and 0·1341 H_2O. C = 63·93; H = 8·42.
Dihydroisolauronic acid, $C_9H_{14}O_3$, requires C = 63·53; H = 8·23 per cent.

This distilled acid melted at about 78—84°, dissolved completely in dilute sodium carbonate solution, and, as the analysis shows, consisted of unchanged dihydroisolauronic acid.

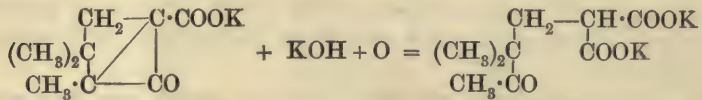
These experiments appear to the author to prove conclusively that *dihydroisolauronic acid is incapable of forming a lactone.*

Fusion of Isolauronic Acid with Potash. Formation of Hydroxy-paratoluic Acid,



The behaviour of isolauronic acid on fusion with potash was investigated, because it was thought probable that in this way a more direct product of hydrolysis and oxidation might be obtained than had been found possible by submitting it to oxidation alone.

It was conceivable, for example, that the reaction might take the following course.



Isolauronic acid (1 gram) was dissolved in strong aqueous potash (10 grams), and the solution, which, on warming, rapidly became dark brown, was gradually heated at 130—140° until the frothing had subsided; the temperature was then raised to 230° for 10 minutes.

On acidifying, a milky solution smelling strongly of isobutyric acid was obtained, and on shaking it, a dark, resinous mass separated; this was extracted five times with ether, the ethereal solution evaporated, and the residue, which on standing overnight partially solidified, boiled with about 200 c.c. of water and filtered. The filtrate, decolorised by boiling with purified animal charcoal, was evaporated to a small bulk on the water bath, and on standing it deposited glistening plates, which were collected, recrystallised twice from water, and analysed, with the following result.

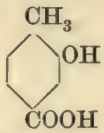
0·1291 gave 0·2978 CO_2 and 0·0642 H_2O. C = 62·91; H = 5·52.

$C_8H_8O_3$ requires C = 63·15; H = 5·26 per cent.

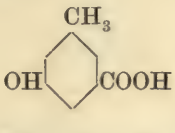
This acid melts at about 203—205° without decomposition, and when cautiously heated sublimes in feathery crystals; it dissolves readily in warm, sparingly in cold water, and crystallises from the hot solution, on slowly cooling, in beautiful, colourless, glistening prisms. When heated with acetic anhydride, it yields an acetyl compound, which crystallises from dilute alcohol in colourless needles and melts at 163—164°, but the amount obtained was too small for analysis.

As the results of the analysis and general properties of the acid clearly showed that it must be an aromatic compound, a search was

made among known hydroxy-acids of this composition, when two acids of similar properties were found, namely,



2-Hydroxyparatoluic acid, m. p. 206—207°.



5-Hydroxymetatoluic acid, m. p. 208.

Mr. J. L. Rose, B.Sc., a student of Owens College, kindly prepared for me a specimen of the former of these acids, using the method described by Weinreich (*Ber.*, 1887, **20**, 981), which consists in sulphonating paratoluic acid and fusing the sulphonic acid with potash. The acid thus obtained, which melted at 206—207°, was digested with acetic anhydride for 1 hour, and when cold mixed with water and allowed to stand until it had completely solidified; this acetate, when purified by recrystallisation from benzene, separated in beautiful, colourless needles which melted at 162°, and gave the following result on analysis.

Found C = 61·99; H = 5·19.

$CH_3 \cdot C_6H_3(O \cdot C_2H_3O) \cdot COOH$ requires C = 61·85; H = 5·16 per cent.

The properties of the acid obtained by fusing isolauronic acid with potash agree, so far as they have been investigated, with those of hydroxyparatoluic acid, but as it is still possible that the acid may be hydroxymetatoluic acid, a specimen of the latter acid is being prepared in order that this point may be decided.

RICHARD CLAY AND SONS, LIMITED, LONDON AND BUNGAY.

OXIDATION OF SULPHOCAMPHYLIC ACID

BY

W. H. PERKIN, JUN.

[From the Transactions of the Chemical Society, 1899.

Oxidation of Sulphocamphylic Acid.

By W. H. Perkin, jun.

When sulphocamphylic acid is oxidised at 0° with potassium permanganate, the principal product is a beautifully crystalline substance which melts at 254° and, on analysis, gives numbers agreeing with the formula $C_{18}H_{22}O_7$; at 100°, it loses one molecule of water, which is probably water of crystallisation, and is converted into a substance, $C_{18}H_{20}O_6$, which has been named "*dicampherylic acid.*"

Dicampherylic acid is a dibasic acid, as is shown by the analysis of its silver salt, $C_{18}H_{18}Ag_2O_6$, and of its methylic salt, $C_{18}H_{18}(CH_3)_2O_6$, its formula may, therefore, be written $C_{16}H_{18}O_2(COOH)_2$. The acid, furthermore, contains two ketonic groups, since, with hydroxylamine, it yields a dioxime, $C_{14}H_{18}(C{:}NOH)_2(COOH)_2$, and is, by reduction with sodium amalgam, converted into *tetrahydrodicampherylic acid*, $C_{14}H_{18}(CH{\cdot}OH)_2(COOH)_2$; its formula may, therefore, be developed to $C_{14}H_{18}(CO)_2(COOH)_2$. The most interesting property of dicampherylic acid is its decomposition by concentrated sulphuric acid at 85°, when it is converted almost quantitatively into an acid of the formula $C_9H_{10}O_3$.

$$C_{18}H_{20}O_6 = 2C_9H_{10}O_3.$$

The determination of the nature of the acid, $C_9H_{10}O_3$, was found to be a problem of considerable difficulty, but its constitution was ultimately established by the consideration of the following facts.

This acid is a monobasic acid, giving well characterised salts, of which the *silver salt*, $C_9H_9AgO_3$, the beautifully crystalline *methylic salt*, $C_9H_9(CH_3)O_3$, and the *ethylic salt*, $C_9H_9(C_2H_5)O_3$, were analysed, and since, on treatment with acetic anhydride, it is converted into an *acetyl compound*, $C_9H_9(OC_2H_3O)O_2$, it is evident that it is a hydroxycarboxylic acid of the composition $C_8H_8(OH){\cdot}COOH$.

When exposed to the action of bromine vapour, the acid, by substitution, yields a *dibromo-derivative*, $C_8H_6Br_2(OH){\cdot}COOH$, in which the bromine is so firmly united that boiling with potash does not eliminate it, a behaviour which indicates that the acid belongs to the aromatic

series. This supposition is confirmed by the fact that nitric acid converts the acid into a *dinitro-derivative*, $C_8H_6(NO_2)_2(OH)\cdot COOH$, an interesting substance which behaves like a dibasic acid, since its silver salt, which crystallises in dark red needles, has the formula $C_9H_6Ag_2N_2O_7$, and is evidently produced by the substitution, not only of the hydrogen of the carboxyl group, but also that of the hydroxyl group, by silver, that is, its formula may be written

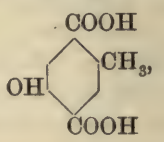
$$C_8H_6(NO_2)_2(OAg)\cdot COOAg.$$

This behaviour is quite usual in aromatic hydroxy-acids containing two nitro-groups. Thus, for example, 3 : 5-dinitrohydrocumaric acid, $OH\cdot C_6H_2(NO_2)_2\cdot CH_2\cdot CH_2\cdot COOH$, yields a dibasic silver salt crystallising in dark red needles, and 1 : 3 : 5-dinitroparahydroxybenzoic acid, $OH\cdot C_6H_2(NO_2)_2\cdot COOH$, a dibasic salt crystallising in brown needles. From these results, it was evident that the acid $C_9H_{10}O_3$ was either a hydroxydimethylbenzoic acid, $OH\cdot C_6H_2(CH_3)_2\cdot COOH$, or a hydroxyethylbenzoic acid, $OH\cdot C_6H_3(C_2H_5)\cdot COOH$; it could not be a hydroxyhydrocumaric acid, $OH\cdot C_6H_4\cdot CH_2\cdot CH_2\cdot COOH$, since the three isomeric (*o*-, *m*-, *p*-) forms of this acid are known, and melt respectively at 83°, 111°, and 129°, whereas the acid $C_9H_{10}O_3$ melts at 204°. In order to determine whether it contained an ethyl group or two methyl groups, it was decided to endeavour to oxidise the acid. Before doing this, however, it was necessary to protect the hydroxyl group by converting it into a methoxy-group, and this was readily accomplished by treating the methylic salt of the acid with sodium methylate and methylic iodide in the usual way. The oily methylic salt,

$$OCH_3\cdot C_8H_8\cdot COOCH_3,$$

thus formed yielded, on hydrolysis, the corresponding *methoxy-acid*, $OCH_3\cdot C_8H_8\cdot COOH$, and this, on oxidation with permanganate, was almost quantitatively converted into an acid of the formula $OCH_3\cdot C_7H_5(COOH)_2$, showing that the original acid, $C_9H_{10}O_3$, must have contained two methyl groups, one of which had been converted into COOH during the oxidation; in short, the acid $C_9H_{10}O_3$ is a dimethylhydroxybenzoic acid, $OH\cdot C_6H_2(CH_3)_2\cdot COOH$.

On heating the methoxydibasic acid, $OCH_3\cdot C_7H_5(COOH)_2$, with hydriodic acid, the corresponding hydroxy-acid, $OH\cdot C_7H_5(COOH)_2$, was obtained as a very sparingly soluble, crystalline powder melting at 283°, and giving, in alcoholic solution, an intense reddish-violet coloration with ferric chloride. As these properties are the same as those of the hydroxymethylterephthalic acid of the formula



described by Jacobsen and H. Meyer (*Ber.*, 1883, **16**, 191), the author at first thought that the acids were identical (compare Proc., 1893, **9**, 110).

The experiments up to this stage were completed in 1893, and since then, during the course of a long investigation into the properties of sulphocamphylic acid, some new facts were discovered which made it improbable that this formula could be correct.

The subject was therefore further investigated, and after much labour the relative positions in the hydroxydimethylbenzoic acid, $C_9H_{10}O_3$, and also in the hydroxymethyldicarboxylic acid, $OH \cdot C_6H_2(CH_3)(COOH)_2$, produced by its oxidation have, as the author believes, been clearly established.

In the first place, the acid, $C_9H_{10}O_3$, which melts at 204° and gives no colour with ferric chloride, is isomeric with the already known hydroxydimethylbenzoic acids, as will be seen from the following table, in which the numbers refer to the groups taken in the order $CH_3 : CH_3 : OH : COOH$.

		M. p.	
ortho-Hydroxyparaxylic acid	1 : 2 : 5 : 4	199°	$FeCl_3$, bluish-violet.
ortho-Hydroxymesitylenic acid	1 : 3 : 4 : 5	179	$FeCl_3$, intense blue.
para-Hydroxymesitylenic acid	1 : 3 : 2 : 5	223	$FeCl_3$, brown.
α-Hydroxyxylic acid	1 : 3 : 1 : 4	170	
β- „ „	1 : 4 : 2 : 3	144	
γ- „ „	1 : 4 : 5 : 2	153	

The careful investigation of the acid $C_9H_{10}O_3$, melting at 204°, has clearly established the following points.

1. *The Hydroxyl Group is in the Meta-position relatively to the Carboxyl Group.*—That the acid is not an orthohydroxy-acid is clearly indicated by the fact that it gives no colour with ferric chloride; that it is neither an *ortho*hydroxy- nor a *para*hydroxy-acid is shown by the fact that it may be heated with concentrated hydrochloric acid or hydriodic acid at 200—220° without decomposition, whereas ortho- and para-hydroxy-acids are readily decomposed into the corresponding phenols and carbonic anhydride by this treatment.

2. *The Acid is derived from the Xylenol*, $[(CH_3)_2 : OH = 1 : 2 : 6]$.—When the calcium salt of the acid $C_9H_{10}O_3$ is distilled with lime, it shows the behaviour characteristic of the calcium salts of *meta*-hydroxy-acids, namely, decomposition takes place with great difficulty, and only at an exceedingly high temperature. The distillate contains a xylenol, which crystallises from water in long, colourless needles, and the aqueous solution of which gives, with ferric chloride, a distinct, although not intense, bluish-violet coloration; it melts at 75° and distils constantly at 218°. The identity of this xylenol was, with difficulty, established in the following way. All the six possible

xylenols, $C_6H_3(CH_3)_2 \cdot OH$, have been prepared and carefully investigated, so that their properties are well known; and in order to clearly show how the constitution of the xylenol from the acid $C_9H_{10}O_3$ was proved, a short table of the properties of the xylenols is appended, the numbers referring to the groups in the order $CH_3 : CH_3 : OH$.

I.....	1:3:5	b. p. 219·5°	m. p. 68°	$FeCl_3$, no colour.
II.....	1:2:6	,, 218	,, 75	,, violet.
III.....	1:4:2	,, 211·5	,, 75	,, no colour.
IV	1:2:4	,, 225	,, 65	,, not stated.
V.....	1:3:4	,, 211·5	,, 26	,, blue.
VI.....	1:3:2	,, 212	,, 49	,, not stated.

Three of these xylenols, namely, Nos. III, IV, and V, were obtained from Schuchardt, and after very careful purification found to be different from the author's xylenol, as, indeed, the melting and boiling points would indicate. Since, again, both the melting point and boiling point of No. VI differ markedly from those of the author's xylenol, there remain only Nos. I and II as possibly representing its constitution, and of these, No. II is the more probable, since this melts and boils at exactly the same temperatures, whereas No. I has a lower melting point, and is stated to give no coloration with ferric chloride. As, however, very slight traces of impurity considerably depress the melting point of the xylenols, and as the colour with ferric chloride is not pronounced in the case of any one of them, it was necessary to obtain further evidence before deciding this question of identity. Fortunately, there is a wide difference in the melting points of the tribromo-xylenols derived from Nos. I and II, that from the former melting at 166°, whereas that from the latter melts at 184°, and on trying the experiment with the author's xylenol it was found that its tribromo-derivative melted sharply at 184°; there can, therefore, be no doubt that the constitution of this xylenol is represented by the formula $C_6H_3(CH_3)_2 \cdot OH = 1:2:6$.

Since, then, the acid, $OH \cdot C_6H_2(CH_3)_2 \cdot COOH$, from which this xylenol was obtained is a metahydroxy-acid, it can only have the formula $C_6H_2(CH_3)_2(COOH) \cdot OH = 1:2:4:6$; that is, it is *metahydroxyparaxylic acid*, and closely allied to *orthohydroxyparaxylic acid*, [1:2:4:5], which Reuter (*Ber.*, 1878, **11**, 30) prepared by fusing pseudocumenesulphonic acid with caustic potash (compare Jacobsen, *Ber.*, 1899, **12**, 436). This is the second occasion on which a derivative of pseudocumene has been obtained indirectly from sulphocamphylic acid, as Koenigs and Meyer (*Ber.*, 1894, **27**, 3468, [compare Trans., 1898, p. 840) found previously that isolauronic acid was readily converted into paraxylic acid by the action of sulphuric acid.

The hydroxy-dibasic acid, produced indirectly by the oxidation of

metahydroxyparaxylic acid as described above, is evidently an ortho-hydroxy-acid, since its alcoholic solution gives an intense blue coloration with ferric chloride; it can, therefore, only be a hydroxymethylterephthalic acid of the formula

$$OH\cdot C_6H_2(CH_3)\cdot COOH_2\ [CH_3\cdot COOH : OH : COOH = 1 : 3 : 5 : 6],$$

and the difference between this formula and that originally assigned to this acid (see p. 176) is simply in the position of the hydroxyl group.

Unfortunately, like so many other instances in which benzene compounds have been obtained from camphor and its derivatives, the formation of metahydroxyparaxylic acid throws very little light on the constitution of dicampherylic acid, from which it is so readily produced, and although it would be easy to suggest a formula for the latter acid, the author prefers not to do so until further experimental data are forthcoming.

With regard to the formation of such benzene derivatives as xylene, cymene, pseudocumene, carvacrol, acetylortho-xylene, and others from camphor, and of derivatives of paratoluic acid and paraxylic acid from camphoric acid, the author entirely shares the opinion, somewhat differently expressed by Aschan,* namely, that until we understand the extraordinary mechanism of the production of these benzene derivatives, their formation is of little value in determining the constitution of the substances from which they are derived.

The author is much indebted to Messrs. B. Prentice, J. L. Heinke, F. H. Lees, and others for their valuable assistance in the experimental part of this investigation.

The author also wishes to state that the heavy cost of the very large amount of material used in this research was to a very considerable extent covered by repeated large grants from the Government Grant Fund of the Royal Society.

Experimental.

Oxidation of Sulphocamphylic Acid. Formation of Dicampherylic Acid, $C_{18}H_{20}O_6 + H_2O$.

In carrying out this oxidation, sulphocamphylic acid in quantities of 50 grams was dissolved in about 1 litre of water, the solution neutralised with potassium carbonate, and transferred to a flat porcelain basin in which a turbine was fitted. The solution was cooled to 0° by adding powdered ice, and a cold saturated solution

* Structur und stereochemische Studien in der Camphergruppe; Helsingfors, 1895, p. 17.

of potassium permanganate run in slowly until the colour, which instantly disappears at first, just remained permanent, care being taken that the whole was well stirred and the temperature kept below 2° during the operation. The product from several such oxidations was filtered, the filtrate and washings of the manganese precipitate evaporated to a small bulk, and the concentrated yellow solution acidified and allowed to stand overnight; the yellow, crystalline precipitate which had separated was collected, washed with water, and purified by repeated crystallisation from dilute acetic acid; the magnificent, lemon-yellow prisms thus obtained, after standing for some days on a porous tile in contact with air, gave the following results on analysis.

0·1216 gave 0·2757 CO_2 and 0·0712 H_2O. C = 61·83; H = 6·50.
0·1410 „ 0·3190 CO_2 „ 0·0806 H_2O. C = 61·70; H = 6·35.
0·1524 „ 0·3448 CO_2 „ 0·0894 H_2O. C = 61·70; H = 6·51.
$C_{18}H_{22}O_7$ requires C = 61·71; H = 6·28 per cent.

These crystals, when heated for a long time at 100°, gradually lose water, a change which takes place rapidly at 120—130°. 1·0952 grams of the substance, dried in the air, lost 0·0610 gram at 100°, or 5·47 per cent., whereas the calculated loss, supposing $C_{18}H_{22}O_7$ to be converted into $C_{18}H_{20}O_6$ at 100°, is 5·14 per cent. An analysis of the substance, dried at 120° until of constant weight, gave the following result.

0·1496 gave 0·3571 CO_2 and 0·0851 H_2O. C = 65·10; H = 6·32.
$C_{18}H_{20}O_6$ requires C = 65·06; H = 6·02 per cent.

The molecular weight of this substance was determined by the cryoscopic method, when it was found that 0·8010 gram, dissolved in 36·1 grams of acetic acid, depressed the melting point 0·26°, this corresponding with a molecular weight 332, whereas the molecular weight of $C_{18}H_{20}O_6$ is 332 and of $C_{18}H_{22}O_7$ 350.

On long standing in an uncorked flask, the solution used in this determination deposited a mass of slender, colourless needles which looked like threads of asbestos and quite unlike the hard prisms in which the substance $C_{18}H_{22}O_7$ usually crystallises. An analysis showed, however, that the crystals had the composition $C_{18}H_{22}O_7$.

0·1028 gave 0·2328 CO_2 and 0·06 H_2O. C = 61·76; H = 6·48.
$C_{18}H_{22}O_7$ requires C = 61·71; H = 6·28 per cent.

These results, taken together with those described in the following pages, show that the product of the oxidation of sulphocamphylic acid is a substance of the formula $C_{18}H_{20}O_6$, which crystallises with water in prisms of the composition $C_{18}H_{22}O_7$.

This compound, which has been named *dicampherylic acid*, melts at about 254°, and is readily soluble in alcohol, acetone, acetic acid, and ethylic acetate, but only very sparingly in benzene; it is almost insoluble in cold water, although, in a finely divided state, it dissolves appreciably in boiling water, and separates on cooling in almost colourless, prismatic crystals. It dissolves readily in dilute sodium carbonate, and, although the well-cooled solution does not decolorise permanganate, it does so readily on warming.

Dicampherylic acid dissolves readily in warm, concentrated nitric acid, and, on boiling, oxidation takes place so slowly that even after 10 minutes the addition of water causes a large quantity of the substance to separate unchanged. Fuming hydriodic acid dissolves the finely-powdered crystals easily, and if, after boiling for a short time, the bulk of the hydriodic acid is distilled off, the residue, on mixing with water, deposits a heavy, dark brown oil which becomes colourless on the addition of sulphurous acid and smells like isoamylic iodide.

Salts of Dicampherylic Acid.

That this acid is a dibasic acid was first shown by titrating a weighed quantity of the anhydrous crystals with standard alkali, when it was found that 0·4416 required for neutralisation 0·1495 gram KOH, or 33·8 per cent., whereas a dibasic acid of the formula $C_{18}H_{20}O_6$ requires 33·7 per cent.

The *silver salt* was obtained as a white, gelatinous precipitate on adding silver nitrate to a warm, neutral solution of the ammonium salt, the precipitate on warming with much water for about an hour becomes crystalline, and is then readily filtered and washed. The analyses seem to show that this salt, after drying over sulphuric acid in a desiccator, has the formula $C_{18}H_{20}Ag_2O_7$, and that at 120—130° it loses water, and then has the formula $C_{18}H_{18}Ag_2O_6$.

The silver salt, dried over sulphuric acid in a desiccator, gave the following results on analysis.

0·2054 gave 0·2833 CO_2, 0·0696 H_2O, and 0·0790 Ag. C = 37·66; H = 3·77; Ag = 38·46.

0·2469 gave 0·3420 CO_2, 0·0746 H_2O, and 0·0953 Ag. C = 37·77; H = 3·36; Ag = 38·58.

0·3390 gave, on ignition, 0·1302 Ag. Ag = 38·41.

$C_{18}H_{20}Ag_2O_7$ requires C = 38·29. H = 3·55; Ag = 38·29 per cent.

This salt may be heated at 120—130° without decomposition, and after its weight had become constant it was analysed.

0·2260 gave 0·3223 CO_2, 0·0681 H_2O, and 0·0887 Ag. C = 38·89; H = 3·35; Ag = 39·24.

0·22, on ignition, gave 0·0860 Ag. Ag = 39·09.

$C_{18}H_{18}Ag_2O_6$ requires C = 39·56; H = 3·30; Ag = 39·56 per cent.

A neutral solution of the ammonium salt of dicampherylic acid gives a heavy, white precipitate with lead acetate, but no precipitate with barium, calcium, or zinc chlorides; copper acetate gives no precipitate in the cold, but on boiling a light blue, crystalline, copper salt separates.

Methylic Dicampherylate, $C_{18}H_{18}(CH_3)_2O_6$.—This salt was prepared by two different methods.

1. The dry silver salt of the acid was digested for 2 hours with ether and excess of methylic iodide, and the ethereal solution filtered; the residue was extracted repeatedly with ether, and the combined ethereal solutions evaporated to a small bulk. On standing, beautiful crystals separated which, after crystallisation from benzene, melted at 226—227°.

2. The acid, dissolved in methylic alcohol, was mixed with concentrated sulphuric acid and heated to boiling on a water-bath for a few minutes; on cooling, glistening crystals separated, which, after collecting, and recrystallising from benzene, melted at 226—227°. This substance, which, like all the derivatives of dicampherylic acid, is very difficult to burn, was analysed, with the following results.

I. 0·1692 gave 0·4120 CO_2 and 0·1040 H_2O. C = 66·42; H = 6·83.
II. 0·1652 „ 0·4011 CO_2 „ 0·0996 H_2O. C = 66·22; H = 6·69.
III. 0·1663 „ 0·4027 CO_2 „ 0·1007 H_2O. C = 66·04; H = 6·73.

$C_{18}H_{18}(CH_3)_2O_6$ requires C = 66·66; H = 6·66 per cent.

In No. I, the methylic salt used was prepared from the silver salt, and in Nos. II and III from the acid by treatment with methylic alcohol and sulphuric acid.

Action of Hydroxylamine on Dicampherylic Acid.

In studying the action of hydroxylamine on dicampherylic acid, the pure acid (2 grams), dissolved in dilute potash (6 grams), was mixed with hydroxylamine hydrochloride (2 grams), and acidified after 12 hours, when the nearly pure oxime separated in white flocks.* The whole was extracted with much ether, the ethereal solution rapidly† dried

* In this form, the oxime is readily soluble in ether, and also in warm water, but after crystallisation from ether, it becomes almost insoluble, both in this solvent and in water.

† If this operation is not very quickly performed, the oxime is apt to separate on the lumps of calcium chloride.

with calcium chloride, filtered, and allowed to stand either as it was, or, better, after concentrating somewhat, when the oxime separated in crystalline crusts. These crusts, after washing with ether, gave the following results on analysis.

I. 0·1420 gave 0·3090 CO_2 and 0·0830 H_2O. C = 59·35 ; H = 6·50.
II. 0·1548 „ 0·3362 CO_2 „ 0·0914 H_2O. C = 59·23 ; H = 6·57.
III. 0·1699 „ 0·3663 CO_2 „ 0·0986 H_2O. C = 58·80 ; H = 6·44.
IV. 0·1608 „ 0·3487 CO_2 „ 0·0937 H_2O. C = 59·14 ; H = 6·47.
V. 0·2602 „ 17·4 c.c. nitrogen at 18° and 758 mm. N = 7·70.

Other nitrogen determinations gave N = 6·90, 7·30, and 7·05.

$C_{18}H_{22}N_2O_6$ requires C = 59·66 ; H = 6·07 ; N = 7·73 per cent.

This substance is, therefore, the dioxime of dicampherylic acid produced according to the equation

$$C_{18}H_{20}O_6 + 2NH_2{\cdot}OH = C_{18}H_{20}O_4(N{\cdot}OH)_2 + 2H_2O.$$

When heated in a capillary tube, the oxime turns brown at 210—220°, and gradually becomes darker as the temperature rises, but does not melt completely at 250°. It is almost insoluble in ether and most organic solvents, but dissolves in concentrated hydrochloric acid, and is reprecipitated unchanged when the solution is diluted with water and warmed; it dissolves also in caustic potash solution, and is reprecipitated unchanged by hydrochloric acid.

Action of Acetic Anhydride on the Dioxime.—The pure dioxime dissolves slowly, but completely in cold acetic anhydride, and if the solution is allowed to remain in contact with air, a crystalline cake gradually forms; this, after recrystallisation from dilute acetic acid, gave the following results on analysis.

0·1524 gave 0·3130 CO_2 and 0·0800 H_2O. C = 56·0 ; H = 5·83.
0·1277 „ 0·2640 CO_2 „ 0·0702 H_2O. C = 56·38 ; H = 6·11.
0·2106 „ 12·4 c.c. nitrogen at 18° and 742 mm. N = 6·63.
$C_{20}H_{26}N_2O_8$ requires C = 56·87 ; H = 6·13 ; N = 6·63 per cent.

This substance, which is doubtless the *acetate of the dioxime*, $C_{18}H_{22}N_2O_6,C_2H_4O_2$, melts at 184°, and crystallises from dilute acetic acid in microscopic needles; when heated at 190—200°, it froths up and emits an odour of acetic anhydride. Dilute potash hydrolyses this acetate, and on acidifying and extracting with ether in the usual way, the characteristic crusts of the regenerated dioxime are obtained.

0·3153 gave 22·5 c.c. nitrogen at 22° and 758 mm. N = 8·06.
$C_{18}H_{22}N_2O_6$ requires N = 7·73 per cent.

Action of Phenylhydrazine on Dicampherylic Acid.

When dicampherylic acid (3·5 grams) is mixed with freshly-distilled phenylhydrazine (5 grams) and glacial acetic acid (10 grams), and the mixture heated on the water-bath, reaction sets in in a short time with evolution of gas, the liquid soon becomes dark-red, and after 20 minutes crystals begin to separate. As soon as the separation appears to be complete, the whole is filtered hot on a platinum cone,* and the crystals washed with acetic acid and recrystallised from this solvent. The ruby-red crystals thus obtained are very difficult to burn, and for this reason several analyses were made, with the following results.

0·1487 gave 0·3736 CO_2 and 0·0820 H_2O. C = 68·50; H = 6·13.
0·1735 „ 0·4333 CO_2 „ 0·0957 H_2O. C = 68·16; H = 6·13.
0·1562 „ 0·3873 CO_2 „ 0·0908 H_2O. C = 67·62; H = 6·46.
0·1963 „ 18·5 c.c. nitrogen at 21° and 753 mm. N = 10·64.

These analytical numbers agree best with the formula $C_{30}H_{34}N_4O_5$, which would be obtained by the combination of 1 mol. of dicampherylic acid and 2 mols. of phenylhydrazine with loss of water, $C_{18}H_{20}O_6 + 2C_6H_5{\cdot}NH{\cdot}NH_2 = C_{30}H_{34}N_4O_5 + H_2O$, or it is possible that it is the dihydrazone of $C_{18}H_{20}O_6$ crystrallising with $1H_2O$.

This substance dissolves in hot acetic acid or alcohol, forming yellow solutions which, on cooling, deposit brilliant, ruby-red crystals. When heated in a capillary tube, it darkens at 230°, and decomposes with evolution of gas and charring at 237°. It dissolves in alkalis and alkali carbonates, forming yellow solutions, which, on acidifying, give a bright yellow precipitate, consisting, apparently, of the unchanged substance.

Reduction of Dicampherylic Acid. Formation of Tetrahydrodicampherylic Acid, $C_{18}H_{24}O_6$.

In order to investigate this reduction, pure dicampherylic acid was dissolved in dilute soda and treated in a flat basin with a large excess of sodium amalgam (5 per cent.), and after 24 hours, the whole was neutralised, filtered, and the filtrate acidified and extracted many times with ether. The ethereal solution, after drying and concentrating, deposited the greater part of the product of reduction in crystalline flakes. These were collected, washed with ether, and analysed.

* The mother liquors when heated with more phenylhydrazine give another crop of crystals.

0·1683 gave 0·3955 CO_2 and 0·1126 H_2O. C = 64·09; H = 7·43.
0·1500 „ 0·3497 CO_2 „ 0·1003 H_2O. C = 63·58; H = 7·42.
0·1615 „ 0·3816 CO_2 „ 0·1080 H_2O. C = 64·44; H = 7·43.
$C_{18}H_{24}O_6$ requires C = 64·28; H = 7·14 per cent.

The determination of the molecular weight of this acid by the boiling point method, using alcohol as the solvent, gave 298, 307, and 296, whereas the calculated molecular weight for $C_{18}H_{24}O_6$ is 336.

Tetrahydrodicampherylic acid melts at about 297—298° with evolution of gas. It is sparingly soluble in methylic and ethylic alcohols and acetic acid in the cold, and in boiling water, and is not readily soluble even in boiling acetic acid; but from its solution in dilute acetic acid it separates, on long standing, in four-sided plates.

Silver Tetrahydrodicampherylate.—When a hot, dilute solution of the ammonium salt of the acid is mixed with silver nitrate, a white precipitate is formed, and if this be rapidly removed with the aid of the pump, the filtrate, on standing, deposits beautiful groups of colourless crystals of a silver salt; this, on analysis, gave the following numbers.

0·2169 gave 0·3070 CO_2, 0·0826 H_2O, and 0·0846 Ag. C = 38·60; H = 4·18; Ag = 39·0.
$C_{18}H_{22}Ag_2O_6$ requires C = 39·27; H = 4·0; Ag = 39·27 per cent.

Fusion of Dicampherylic Acid with Potash.

Fifteen grams of the pure acid was mixed with 50 grams of potash and a little water, and heated at about 120°, when the crystals rapidly dissolved, forming a dark solution, which readily crystallised owing to the separation of a potassium salt. On raising the temperature, the liquid became dark brown, and then red, and after much frothing suddenly solidified at about 165°, a peculiar aromatic smell being noticeable; more potash (20 grams) was then added, and the temperature gradually raised, until, at 250°, the frothing had entirely ceased. The melt was dissolved in water, acidified, and extracted 10 times with ether, the ethereal solution evaporated, and the viscid residue, which smelt strongly of fatty acids, distilled in a current of steam. The strongly acid distillate, when neutralised with pure calcium carbonate and concentrated, deposited beautiful, feathery crystals of calcium isobutyrate; these were collected and analysed.

*Determination of Water of Crystallisation.**—0·2426 gram, on heating at 100° until constant, lost 0·0674 gram H_2O = 27·79.

$(C_4H_7O_2)_2Ca + 5H_2O$ requires H_2O = 29·60 per cent.

* Compare Crossley and Perkin, Trans., 1898, **73**, 15.

0·1752 gave 0·1107 $CaSO_4$. Ca = 18·58.
$(C_3H_7 \cdot COO)_2Ca$ requires Ca = 18·67 per cent.

The remainder of the calcium salt was dissolved in water, acidified with hydrochloric acid, and the oily acid which separated extracted with ether; the dried ethereal solution, after the ether had been removed on the water-bath, left an oily residue of isobutyric acid which distilled at 154—155°.

0·1684 gave 0·3347 CO_2 and 0·1368 H_2O. C = 54·21; H = 9·08.
C_3H_7COOH requires C = 54·54; H = 9·09 per cent.

This acid, which is undoubtedly isobutyric acid, is formed in considerable quantities during this fusion, as the amount obtained from 15 grams of dicampherylic acid could hardly have been less than 3 grams.

The residue in the distilling flask, after the isobutyric acid had been removed by steam, contained a flocculent precipitate; this was removed by filtration, and the filtrate extracted five times with ether. The ethereal solution, on evaporation, deposited 9 grams of an almost colourless, thick, oily acid, which showed no signs of crystallising, even after standing for some weeks over sulphuric acid. On analysis, it gave the following numbers.

0·1535 gave 0·3364 CO_2 and 0·0842 H_2O. C = 59·77; H = 6·11.
$C_9H_{10}O_4$ requires C = 59·34; H = 5·50 per cent.

In the hope of obtaining this acid in a crystalline condition, it was converted into its lead salt, by adding lead acetate to its aqueous solution, and the white precipitate, which looked almost crystalline, was suspended in water and decomposed by hydrogen sulphide; the filtrate, after concentration, was extracted with pure ether, &c., in the usual way, and the residue, on being allowed to remain over sulphuric acid in a vacuum desiccator, left a colourless, syrupy acid which, on analysis, gave the following results.

0·1753 gave 0·3785 CO_2 and 0·0953 H_2O. C = 58·88; H = 6·05.
0·1418 „ 0·3086 CO_2 „ 0·0774 H_2O. C = 59·35; H = 6·05.
$C_9H_{10}O_4$ requires C = 59·34; H = 5·50 per cent.

The *silver salt*, which was obtained as a white, amorphous precipitate on adding silver nitrate to a neutral solution of the ammonium salt, gave the following results on analysis.

0·2157 gave 0·2184 CO_2, 0·0469 H_2O, and 0·1173 Ag. C = 27·61; H = 2·41; Ag = 54·38.
$C_9H_8Ag_2O_4$ requires C = 27·28; H = 2·02; Ag = 54·54 per cent.

This acid, which appears to have the formula $C_7H_8(COOH)_2$, is very

readily soluble in water; when heated, it gives a yellow distillate which is insoluble in cold water, but dissolves on boiling, and therefore very probably consists of the anhydride. The solution of the acid in sodium carbonate does not decolorise permanganate at ordinary temperatures except on long standing.

It should be mentioned that, in one experiment on the fusion of dicampherylic acid with potash, a small quantity of an acid was obtained which was almost insoluble in water, and only very sparingly soluble in boiling glacial acetic acid. This acid, which crystallised from acetic acid in needles and melted above 300°, was at first thought to be terephthalic acid, but this is not the case, since its methylic salt is a syrup.

Metahydroxyparaxylic Acid, $C_6H_2(CH_3)_2(COOH)\cdot OH$ [= 1 : 2 : 4 : 6].

This acid, as stated in the introduction, is formed by the action of concentrated sulphuric acid at 85° on dicampherylic acid. The finely-divided acid dissolves readily in warm, concentrated sulphuric acid, forming a yellow solution which, if heated at 80—85°, gradually becomes darker, the decomposition of the dicampherylic acid being complete in about 10 minutes. On pouring the product into water, an ochreous precipitate separates which is collected on the pump, washed well with water, dissolved in dilute sodium carbonate, boiled with animal charcoal, filtered, and the acid reprecipitated. The now almost colourless acid is further purified by recrystallisation, first from glacial acetic acid, and then from water.

0·1462 gave 0·3483 CO_2 and 0·0803 H_2O. C = 64·97; H = 6·10.
0·1402 ,, 0·3360 CO_2 ,, 0·0773 H_2O. C = 65·36; H = 6·13.
0·1268 ,, 0·3023 CO_2 ,, 0·0721 H_2O. C = 65·02; H = 6·31.
$C_9H_{10}O_3$ requires C = 65·06; H = 6·03 per cent.

Metahydroxyparaxylic acid melts at 203—204°, and when strongly heated, as, for example, during the combustion, a portion chars, but the main quantity sublimes in beautiful, colourless crystals. It is readily soluble in alcohol and ether, moderately so in hot water and in glacial acetic acid, but only sparingly in chloroform, light petroleum, benzene, carbon bisulphide, and cold water; its aqueous solution gives no coloration with ferric chloride. From glacial acetic acid, it crystallises beautifully in nearly colourless, glistening plates, which, on exposure to the air, become opaque and chalky, a change which takes place rapidly at 100°; from water, the acid also crystallises well. Hydroxyparaxylic acid does not react with hydroxylamine, and is not reduced by sodium amalgam at the ordinary temperature, or when its solution in hydriodic acid is boiled for some time; at 200—220°, however,

fuming hydriodic acid and phosphorus slowly attack it, with formation of a small quantity of a neutral substance of phenolic nature, but even at this temperature most of the acid remains undecomposed. The great stability of the acid is furthermore clearly shown from the following experiment.

1·5 grams of the pure acid was heated with 10 c.c. of concentrated hydrochloric acid at 230—235° for 8 hours; the tube contained a good deal of charcoal, and the greenish liquid, which had a phenolic odour, was filled with long, silky needles like asbestos threads; these crystals were collected and purified by dissolving in potash, filtering, and reprecipitating with hydrochloric acid; the substance then melted at 202°, and consisted of unchanged hydroxyparaxylic acid, as the following analysis shows.

0·1395 gave 0·3320 CO_2 and 0·0778 H_2O. C = 64·92; H = 6·19.
$C_9H_{10}O_3$ requires C = 65·06; H = 6·03 per cent.

The amount of acid recovered in this experiment was 1·1 grams.

Salts of Hydroxyparaxylic Acid.

The *silver salt*, $C_9H_9AgO_3$, was obtained, on adding silver nitrate to a neutral solution of the ammonium salt, as a white, amorphous precipitate. It decomposes readily on heating, yielding a beautifully crystalline sublimate. The following results were obtained on analysis.

0·1736 gave 0·2486 CO_2, 0·0548 H_2O, and 0·0680 Ag. C = 39·05; H = 3·51; Ag = 39·18.
0·1562 gave 0·0617 Ag. Ag = 39·50.
$C_9H_9AgO_3$ requires C = 39·56; H = 3·30; Ag = 39·56.

The neutral solution of the ammonium salt of hydroxyparaxylic acid gives no precipitate with *calcium** or *barium* chlorides.

Methylic Hydroxyparaxylate, $OH\cdot C_6H_2(CH_3)_2\cdot COOCH_3$.—In order to prepare this salt, the acid (22 grams), dissolved in methylic alcohol (150 c.c.), was mixed with concentrated sulphuric acid (40 c.c.) and heated to boiling for half an hour; more sulphuric acid (10 c.c.) was then added, the boiling continued for half an hour, and the whole allowed to stand overnight. The beautiful, striated, leaf-like crystals which separated were collected with the aid of the pump, and, after washing with water and drying at 100°, were found to weigh 13·8 grams. The brown mother liquors, on diluting with water, deposited a brown oil which, on shaking and stirring, slowly solidified; this crude product, after washing and drying on a porous plate at 100°,

* For a description of the calcium salt of hydroxyparaxylic acid, see p. 192.

weighed 7·5 grams. Each portion was separately crystallised from benzene, and in this way 17 grams of the pure methylic salt was obtained, showing that the acid is easy to etherify.

0·1763 gave 0·4300 CO_2 and 0·1087 H_2O. C = 66·52; H = 6·85.
0·1544 „ 0·3772 CO_2 „ 0·0939 H_2O. C = 66·67; H = 6·76.
$C_{10}H_{12}O_3$ requires C = 66·66; H = 6·66 per cent.

Methylic hydroxyparaxylate melts at 148—149°, and in its other properties closely resembles the corresponding ethylic salt.

Ethylic hydroxyparaxylate, $OH \cdot C_6H_2(CH_3)_2 \cdot COOC_2H_5$.—This was prepared by treating the acid with ethylic alcohol and sulphuric acid in the same way as the methylic salt.

The colourless needles obtained by crystallisation from light petroleum melted at 134—135°, and gave the following results on analysis.

0·1309 gave 0·3270 CO_2 and 0·0891 H_2O. C = 68·13; H = 7·56.
0·1590 „ 0·3962 CO_2 „ 0·1010 H_2O. C = 67·94; H = 7·06.
$C_{11}H_{14}O_3$ requires C = 68·04; H = 7·22 per cent.

Ethylic hydroxyparaxylate is readily soluble in alcohol and benzene, but rather sparingly in light petroleum; its solution in alcohol gives no coloration with ferric chloride.

It is insoluble in sodium carbonate, but dissolves readily in caustic potash solution, and is reprecipitated unchanged on the addition of acid. When heated in small quantities, it distils unchanged.

Acetoxyparaxylic Acid, $C_6H_2(CH_3)_2(OC_2H_3O) \cdot COOH$.

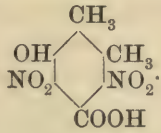
In order to prepare this substance, hydroxyparaxylic acid (1 gram) was boiled with acetic anhydride (10 grams) in a reflux apparatus for half an hour, and the product, when cold, was shaken with water until the excess of anhydride had been removed.

The acetyl compound, which separated as a crystalline cake, was purified by recrystallisation, first from methylic alcohol and then from benzene.

0·1556 gave 0·3612 CO_2 and 0·0810 H_2O. C = 63·30; H = 5·78.
0·1642 „ 0·3805 CO_2 „ 0·0870 H_2O. C = 63·19; H = 5·88.
$C_{11}H_{12}O_4$ requires C = 63·46; H = 5·77 per cent.

Acetoxyparaxylic acid crystallises in colourless, stellate groups, melts at 141—142°, and when rapidly heated in small quantities it distils with only very slight decomposition. It is readily soluble in benzene, alcohol, and ethylic acetate, but almost insoluble in light petroleum; it dissolves with difficulty in, and is only very slowly hydrolysed by,

boiling water, but is readily decomposed by boiling with potassium carbonate solution, and, on acidifying, pure hydroxyparaxylic acid separates.

Dinitrohydroxyparaxylic Acid,  .

When pure hydroxyparaxylic acid is added, in small quantities at a time, to strong nitric acid, it hardly dissolves, and no change takes place until the mixture is gently warmed, when suddenly a vigorous action sets in, the substance passes into solution, and each fresh quantity added dissolves with a slight hissing sound and abundant evolution of red fumes. In a short time, beautiful, yellow crystals separate, and after cooling and mixing with an equal bulk of water, further precipitation takes place. The yellow crystals were collected, washed with water, recrystallised from this solvent and analysed, with the following results.

0·1818 gave 0·2838 CO_2 and 0·0562 H_2O. C = 42·57; H = 3·43.
0·1637 „ 0·2535 CO_2 „ 0·0496 H_2O. C = 42·23; H = 3·36.
0·1996 „ 19·2 c.c. nitrogen at 22° and 754 mm. N = 10·81.
$OH\cdot C_6(CH_3)_2(NO_2)_2\cdot COOH$ requires C = 42·19; H = 3·12; N = 10·94 per cent.

Dinitrohydroxyparaxylic acid is readily soluble in alcohol, acetone, ethylic acetate, and acetic acid, moderately so in hot water, but only sparingly in cold water, benzene, and chloroform. It crystallises from water in glistening, yellow plates, and dissolves in dilute sodium carbonate, forming a deep orange solution. When heated in a capillary tube, it darkens at 195°, and decomposes rapidly at 203—205° with evolution of gas.

Salts of Dinitrohydroxyparaxylic Acid.

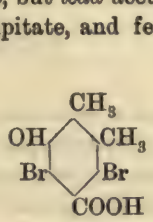
The Silver Salt, $OAg\cdot C_6(CH_3)_2(NO_2)_2\cdot COOAg$.—When silver nitrate is added to a moderately concentrated and slightly alkaline solution of the ammonium salt of the acid, no precipitate is produced at first, but, on standing, a splendid, dark purple, crystalline silver salt separates, which, under the microscope, is seen to consist of fern-like groups of needles. As this salt appeared to be explosive, the silver was determined by heating the substance with nitric acid and hydrochloric acid in a sealed tube at 180° and weighing the silver chloride formed.

0·1466 gave 0·0892 AgCl. Ag = 45·70.
$C_9H_6Ag_2N_2O_7$ requires Ag = 45·95 per cent.

This analysis shows that, in the formation of this salt, the hydrogen of the hydroxyl group, as well as that of the carboxyl group, has been replaced by silver (see p. 176). This silver salt is moderately easily soluble in warm water, and may be recrystallised from this solvent, but, apparently, with a good deal of decomposition.

The faintly alkaline, dilute, orange-coloured solution of the ammonium salt of dinitrohydroxyparaxylic acid gives no precipitate with *copper acetate*, *barium chloride*, or *zinc acetate*, but *lead* acetate produces a very sparingly soluble, heavy, yellow precipitate, and ferric chloride a brownish-red precipitate.

Dibromhydroxyparaxylic Acid,



The action of bromine on hydroxyparaxylic acid was investigated in the following way: 3·9608 grams of the pure, finely powdered acid was exposed in a glass dish to the action of bromine vapour for 12 hours, during which time much hydrogen bromide was produced; after removing the excess of bromine by exposure over solid potash in a vacuum desiccator, it was found that 3·6932 grams of bromine had been absorbed. Representing the reaction by the equation,

$$C_9H_{10}O_3 + 2Br_2 = C_9H_8Br_2O_3 + 2HBr,$$

the increase in weight should have been 3·769 grams.

A determination of the bromine in this crude substance gave the following result.

0·2378 gram gave 0·2698 AgBr. Br = 48·27.

$C_9H_8Br_2O_3$ requires Br = 49·38 per cent.

It is difficult to crystallise the crude substance, and the only way this could be accomplished was to dissolve it in a little methylic alcohol, add a good deal of chloroform, and evaporate to a small bulk to remove most of the methylic alcohol; if, now, more chloroform is added and, after rapidly concentrating, the liquid is allowed to stand, the supersaturated solution rapidly deposits well-shaped, prismatic crystals, which, on analysis, gave the following results.

0·1836 gave 0·2246 CO_2 and 0·0428 H_2O. C = 33·37; H = 2·58.

0·3218 „ 0·3726 AgBr. Br = 49·25.

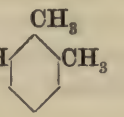
$C_9H_8Br_2O_3$ requires C = 33·33; H = 2·47; Br = 49·38 per cent.

Dibromhydroxyparaxylic acid melts at 204—205°, and is very readily soluble in alcohol, but only sparingly in chloroform; when pure, it crystallises well from dilute alcohol.

It is a very stable substance, and may be boiled for some time with caustic potash without decomposing.

A determination of the molecular weight of this bromo-acid by Raoult's method, using acetic acid as the solvent, gave M = 333, whereas the value calculated from the formula $C_9H_8Br_2O_3$ is 324.

1 : 2-*Xylenol*(6)



This xylenol is produced, as explained in the introduction, when the calcium salt of hydroxyparaxylic acid is distilled with lime.

The calcium salt was prepared by boiling finely divided hydroxyparaxylic acid (30 grams) with water and a slight excess of pure calcium carbonate, filtering, and evaporating nearly to dryness, when, on standing, the calcium salt separated in warty masses.

The dried salt was finely powdered, mixed intimately with slaked lime (50 grams), and distilled in small quantities from small retorts over a blow-pipe, as great heat is necessary to bring about the decomposition. The distillate, which was an aqueous liquid containing dark-coloured, semi-solid masses and smelling very strongly of phenol, was mixed with a slight excess of caustic soda, decolorised by boiling with animal charcoal, filtered, and the filtrate acidified with hydrochloric acid. The oily precipitate solidified rapidly and almost completely, and after collecting, washing, and spreading on a porous plate, an almost colourless, crystalline mass (3 grams) was obtained. On submitting this to distillation, nearly the whole passed over at 218° (760 mm.) as a colourless oil which, on cooling, at once solidified. The distillate, dissolved in a considerable quantity of water at 70°, on slowly cooling, deposited very long, colourless needles, which were dried, first on a porous plate and then at 60°, and analysed.

0·1415 gave 0·4075 CO_2 and 0·1053 H_2O. C = 78·54; H = 8·27.
$C_6H_3(CH_3)_2 \cdot OH$ requires C = 78·69; H = 8·19 per cent.

This substance, which has been found to be 1 : 2-*xylenol*(6), melts at 74—75°, and is moderately soluble in hot water; its cold, saturated, aqueous solution gives a distinct, although not intense, bluish-violet coloration with ferric chloride, and, on standing, the solution rapidly becomes opaque (compare Töhl, *Ber.*, 1885, 18, 2562; Nölting and Forel, *ibid.*, p. 2673).

Tribromo-xylenol, $C_6Br_3(CH_3)_2 \cdot OH$.—This substance, which has already been described by Töhl (*loc. cit.*), was prepared by adding about 0·5 gram of the xylenol obtained in the above experiment, in small

quantities at a time, to 3 grams of bromine, care being taken to moderate the vigorous reaction by cooling; after 2 hours, the product was poured on to a glass dish, and left over potash in a desiccator until the excess of bromine had been removed, the residue being purified by recrystallisation from the dilute alcohol.

0·2840 gave 0·4440 AgBr. Br. = 66·52.

$C_8H_7Br_3O$ requires Br = 66·85 per cent.

This tribromo-xylenol crystallises from dilute alcohol in long, pale-yellow needles which melt at 184°, and it thus agrees in its properties with the tribromo-derivative which Töhl obtained by brominating 1 : 2-xylenol (6).

Methoxyparaxylic Acid, $[(CH_3)_2 : COOH : OCH_3 = 1 : 2 : 4 : 6]$.

With the object of obtaining further information as to the constitution of the acid $C_9H_{10}O_3$, now known to be hydroxyparaxylic acid, it was decided to endeavour to oxidise one or more methyl groups, and in order to do this it was necessary, in the first instance, to protect the hydroxyl group in the usual way, namely, by substituting methyl or ethyl for hydrogen. For this purpose, in the first experiments, the methylic salt of the acid (15 grams) was mixed with a solution of sodium (2 grams) in methylic alcohol and methylic iodide (25 grams), and the mixture heated first at 95—110° for 2 hours, and afterwards at 120—130° for 2 hours. The light-brown product was evaporated on the water-bath, water added, and the heavy oil extracted with ether; the ethereal solution, on evaporation, deposited an oil which did not show any signs of crystallising, and which, doubtless, consisted of the methylic salt of methoxyparaxylic acid, $OCH_3 \cdot C_6H_2(CH_3)_2 \cdot COOCH_3$. This was not analysed, but at once hydrolysed by boiling with excess of methyl alcoholic potash for 2 hours; after evaporating the methylic alcohol, and acidifying the aqueous solution of the residue, a very bulky, white precipitate was obtained, which was purified by recrystallisation from 50 per cent. alcohol.

0·1375 gave 0·3356 CO_2 and 0·0823 H_2O. C = 66·56; H = 6·64.

$C_6H_2(CH_3)_2(OCH_3) \cdot COOH$ requires C = 66·66; H = 6·66 per cent.

Methoxyparaxylic acid melts at 170—171°, and distils at a high temperature, apparently without decomposition. It is very sparingly soluble in hot water, and almost insoluble in cold water; it crystallises from boiling water in woolly masses consisting of fine needles. It is readily soluble in acetic acid, methylic alcohol, chloroform, and ethylic acetate, but only sparingly in carbon bisulphide and light petroleum; it crystallises splendidly from ethylic acetate in long, colourless prisms.

Ethylic Ethoxyparaxylate, $OC_2H_5 \cdot C_6H_2(CH_3)_2 \cdot COOC_2H_5$.

This was prepared by heating ethylic hydroxyparaxylate (2 grams) with sodium (0·26 gram) dissolved in alcohol, and ethylic iodide (5 grams) at 120—130° for 2 hours, evaporating the product on the water-bath, and adding water, when an oil separated which rapidly solidified. The crystalline mass was collected, washed with water, left in contact with porous porcelain until free from oil, and recrystallised from dilute methylic alcohol, when glistening prisms were obtained which gave the following results on analysis.

0·1496 gave 0·3841 CO_2 and 0·1110 H_2O. C = 70·02; H = 8·24.
$C_{13}H_{18}O_3$ requires C = 70·27; H = 8·11 per cent.

Ethylic ethoxyparaxylate melts at 50—51°, and is readily soluble in methylic alcohol, light petroleum, benzene, chloroform, and carbon bisulphide.

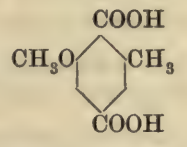
Ethoxyparaxylic Acid, $OC_2H_5 \cdot C_6H_2(CH_3)_2 \cdot COOH$.

When boiled with alcoholic potash, ethylic ethoxyparaxylate is readily hydrolysed, and if the product is mixed with water and evaporated until free from alcohol, the addition of hydrochloric acid to the cold aqueous solution precipitates the acid as a white powder which crystallises from methylic alcohol in beautiful, glistening, prismatic needles.

0·1476 gave 0·3656 CO_2 and 0·0954 H_2O. C = 67·55; H = 7·18.
0·1332 ,, 0·3311 CO_2 ,, 0·0867 H_2O. C = 67·79; H = 7·21.
$C_{11}H_{14}O_3$ requires C = 68·05; H = 7·22 per cent.

Ethoxyparaxylic acid melts at 173—174°; it is sparingly soluble in water and light petroleum, but readily in ethylic and methylic alcohols, benzene, and ethylic acetate.

Methoxymethylterephthalic Acid,



Methoxyparaxylic acid is moderately readily acted on by potassium permanganate in alkaline solution, with formation, in the first instance, of methoxymethylterephthalic acid. In studying this oxidation, the pure acid was dissolved in dilute sodium carbonate, heated to boiling, and a strong, hot solution of potassium permanganate added drop by drop until the colour remained permanent for some minutes; the

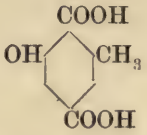
excess of permanganate was then destroyed by the addition of a drop of alcohol, and, after filtration, the filtrate evaporated to a small bulk was acidified with hydrochloric acid.

The bulky, white precipitate which separated at once, was collected, washed well, and crystallised from dilute alcohol.

0·1263 gave 0·2648 CO_2 and 0·0570 H_2O. C = 57·18; H = 5·01.
0·1543 „ 0·3223 CO_2 „ 0·0679 H_2O. C = 56·95; H = 4·88.
$CH_3O{\cdot}C_6H_2(CH_3)(COOH)_2$ requires C = 57·14; H = 4·76 per cent.

Methoxymethylterephthalic acid, when heated in a capillary tube, sinters at about 250°, and melts completely at 267°. It is only sparingly soluble in cold water, but crystallises well from large quantities of boiling water. With ferric chloride, the aqueous solution gives an ochreous precipitate.

Hydroxymethylterephthalic Acid,



In order to prepare this acid, methoxymethylterephthalic acid (3 grams) was boiled with fuming hydriodic acid (30 c.c.) in a reflux apparatus for 2 hours. The liquid, which, on cooling, became filled with crystals, was diluted with water, filtered, and the crystals washed with a little dilute sulphurous acid to remove iodine. In this condition, the crystals are nearly insoluble in water, but if the solution in dilute alkali is heated to boiling and acidified, the acid does not separate at once, and the filtered solution, on slowly cooling, deposits a voluminous precipitate consisting of microscopic needles. The precipitate was collected, washed well, and analysed, with the following result.

0·1512 gave 0·3063 CO_2 and 0·0580 H_2O. C = 55·24; H = 4·26.
$OH{\cdot}C_6H_2(CH_3)(COOH)_2$ requires C = 55·10. H = 4·08 per cent.

Hydroxymethylterephthalic acid melts at 280—283°, and its solution in methylic alcohol gives, with ferric chloride, an intense reddish-violet coloration.

Owens College,
Manchester.

RICHARD CLAY AND SONS, LIMITED, LONDON AND BUNGAY.

ββ-DIMETHYLGLUTARIC ACID AND ITS DERIVATIVES: SYNTHESIS OF CIS- AND TRANS-CARONIC ACIDS.

BY

WILLIAM H. PERKIN, JUN.,

AND

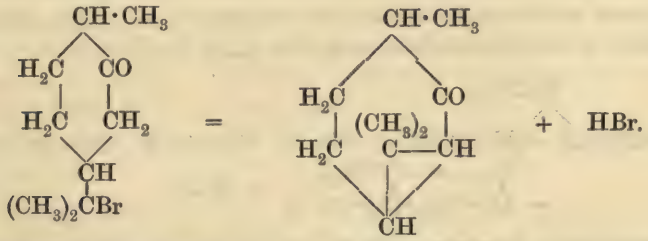
JOCELYN F. THORPE.

From the Transactions of the Chemical Society, 1899.

ββ-Dimethylglutaric Acid and its Derivatives; Synthesis of *cis*- and *trans*-Caronic Acids.

By William H. Perkin, jun., and Jocelyn F. Thorpe.

Carone, $C_{10}H_{16}O$, one of the most important ring ketones in the terpene series, is formed when dihydrocarvone hydrobromide is treated with alcoholic potash, hydrogen bromide being eliminated, a decomposition which, according to G. Wagner,* may be formulated in the following manner.

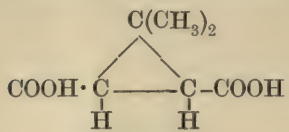


Dihydrocarvone hydrobromide. Carone.

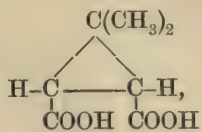
This view of the constitution of carone was considered probable by Baeyer, who, in order to confirm this formula, carried out a number of important experiments on carone, during the course of which he, in conjunction with Ipatieff, investigated the behaviour of this substance on oxidation with permanganate (*Ber.*, 1896, **29**, 2796). It was found that, although carone is very stable towards permanganate at the ordinary temperature, it is moderately readily oxidised at 100°, with formation of two isomeric dibasic acids, $C_5H_8(COOH)_2$, melting at 176° and 212°, which were named caronic acids. The former of these, which is produced in much the larger quantity, readily yielded an anhydride melting at 54—56° when boiled with acetyl chloride, but the other acid was not affected by this treatment

* Compare Baeyer (*Ber.*, 1896, **29**, 5 and 2796).

A careful examination of these acids led Baeyer and Ipatieff to the conclusion that the caronic acids were stereoisomeric modifications of dimethyltrimethylenedicarboxylic acid.

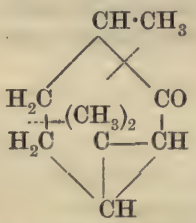


trans-Caronic acid.

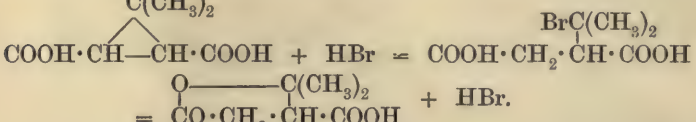


cis-Caronic acid.

and that these were formed by the oxidation of carone at the points indicated by the dotted lines in the formula



That these acids have the same structure and are stereoisomeric seemed probable from their behaviour towards hydrobromic acid at 100°, under which conditions both are converted into terebic acid with disruption of the trimethylene ring (*loc. cit.*, p. 2801).



No mention is, however, made of any attempt to convert the one modification into the other.

In studying this important work, it seemed to us that it would be most interesting to find some means of synthesising the caronic acids, and of thus placing their constitution beyond doubt. This was ultimately accomplished in the way described in this paper.

Some time since, it was shown by Goodwin and Perkin (Trans., 1896, **69**, 1475), that ethylic dimethylacrylate condenses with the sodium derivative of ethylic malonate with formation of ethylic dimethylpropanetricarboxylate,

$$(COOC_2H_5)_2CH\cdot C(CH_3)_2\cdot CH_2\cdot COOC_2H_5,$$

and from this, by hydrolysis and elimination of carbon dioxide, ββ-dimethylglutaric acid, $COOH\cdot CH_2\cdot C(CH_3)_2\cdot CH_2\cdot COOH$, was prepared.

The yield of acid obtained in this way is small, but by substi-

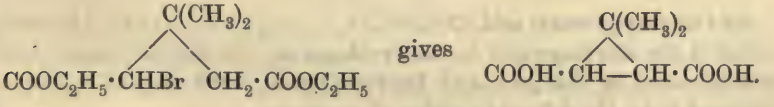
tuting ethylic cyanacetate for ethylic malonate in the condensation with ethylic dimethylacrylate, we now find that the yield of condensation product, which consists of a mixture of some *ethylic α-cyano-ββ-dimethylglutarate*, $COOC_2H_5 \cdot CH(CN) \cdot C(CH_3)_2 \cdot CH_2 \cdot COOC_2H_5$, with much of the *hydrogen ethylic salt*, $COOH \cdot CH(CN) \cdot C(CH_3)_2 \cdot CH_2 \cdot COOC_2H_5$, is more than 80 per cent. of the theoretical, and, as these ethereal salts, on boiling with 50 per cent. sulphuric acid, are quantitatively converted into ββ-dimethylglutaric acid, it is now an easy matter to prepare this acid in quantity.

When the anhydride of dimethylglutaric acid is treated with phosphorus pentabromide and bromine, and the product poured into absolute alcohol, *ethylic bromodimethylglutarate*,

$$COOC_2H_5 \cdot CHBr \cdot C(CH_3)_2 \cdot CH_2 \cdot COOC_2H_5,$$

is produced, together with large quantities of the hydrogen ethylic salt of the same acid, $COOH \cdot CHBr \cdot C(CH_3)_2 \cdot CH_2 \cdot COOC_2H_5$; that the latter should be produced in such quantities is certainly remarkable, and a possible explanation of its formation is given in the experimental part of this paper. When ethylic bromodimethylglutarate is digested with alcoholic potash, hydrolysis and elimination of hydrogen bromide takes place simultaneously, and a mixture of acids is obtained which, by conversion into the ammonium salts and treatment with alcohol, as recommended by Baeyer and Ipatieff (*loc. cit.*, 2978), is easily separated, and found to consist of large quantities of trans-*caronic acid*, some lactone acid of hydroxydimethylglutaric acid (see below), and traces of cis-*caronic acid*.

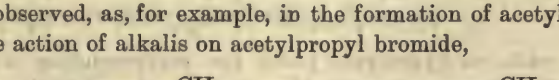
This synthesis of the caronic acids may be represented in the following way.



Hydrogen ethylic bromodimethylglutarate,

$$COOH \cdot CHBr \cdot C(CH_3)_2 \cdot CH_2 \cdot COOC_2H_5,$$

on treatment with alcoholic potash, is quantitatively converted into *trans*-caronic acid, apparently without even traces of the *cis*-modification being formed. The synthesis of a trimethylene compound in the manner represented above is remarkable, but a few similar cases have been observed, as, for example, in the formation of acetyltrimethylene by the action of alkalis on acetylpropyl bromide,



The synthetical caronic acids have been very carefully investigated, and it is shown in the experimental part of this paper that their pro-

perties agree in all respects with those of the acids obtained by Baeyer and Ipatieff from carone, so that there cannot be any doubt as to the identity of the acids produced by these different methods.

One additional point of interest has been discovered, namely, that *trans*-caronic acid is converted into the anhydride of *cis*-caronic acid by the action of acetic anhydride at 220°, a transformation of the *trans*- into the *cis*-modification which was required to clearly show that these two acids are stereoisomeric.

Furthermore, it is shown in this paper that aqueous sodium carbonate hydrolyses the hydrogen ethylic salt of bromodimethylglutaric acid, $COOH\cdot CHBr\cdot C(CH_3)_2\cdot CH_2\cdot COOC_2H_5$, in a manner quite different from alcoholic potash, with formation of the *lactone* of *α-hydroxy-ββ-dimethylglutaric acid*, $\begin{matrix} COOH\cdot C\cdot C(CH_3)_2\cdot CH_2 \\ O\text{———}CO \end{matrix}$, a beautifully crystalline substance which melts at 112° and is isomeric with the caronic acids.

When ethylic bromodimethylglutarate,

$$COOC_2H_5\cdot CHBr\cdot C(CH_3)_2\cdot CH_2\cdot COOC_2H_5,$$

is digested with diethylaniline, hydrogen bromide and ethylic bromide are eliminated and an ethereal salt is obtained, which, on examination, has been found to consist of the ethylic salts of *trans*-caronic acid, and of the *lactone* of hydroxydimethylglutaric acid.

Experimental.

Condensation of Ethylic Dimethylacrylate with the Sodium Derivative of Ethylic Cyanacetate.

ββ-Dimethylglutaric acid, $COOH\cdot CH_2\cdot C(CH_3)_2\cdot CH_2\cdot COOH$, the acid which is the starting-point in the synthesis of the caronic acids, was first prepared by Goodwin and Perkin (Trans., 1896, **69**, 1475), who obtained it by the following series of reactions.

Ethylic dimethylacrylate was, in the first place, digested with the sodium derivative of ethylic malonate in alcoholic solution, when condensation took place with formation of ethylic dimethylpropanetricarboxylate,

$$(COOC_2H_5)_2CH_2 + (CH_3)_2C{:}CH\cdot COOC_2H_5 = (COOC_2H_5)_2CH\cdot C(CH_3)_2\cdot CH_2\cdot COOC_2H_5.$$

This ethereal salt, on hydrolysis, yields the corresponding tribasic acid, which, at 200°, loses carbon dioxide with formation of ββ-dimethylglutaric acid, $COOH\cdot CH_2\cdot C(CH_3)_2\cdot CH_2\cdot COOH$, and from this the anhydride is readily prepared by treatment with acetic anhydride. The yield of the original triethylic salt is unfortunately not good, and

seldom reaches more than 40 per cent. of the theoretical; indeed, the average yield is scarcely more than 28 per cent. Until quite recently, we have prepared all the dimethylglutaric anhydride required for this research by the method devised by Goodwin and Perkin. A few months since, however, we discovered that the yield may be very greatly improved by substituting ethylic cyanacetate for ethylic malonate in the condensation with ethylic dimethylacrylate, the yield of condensation product being increased to at least 80 per cent. by this means.*

Ethylic α-cyano-ββ-dimethylglutarate,

$$COOC_2H_5 \cdot CH(CN) \cdot C(CH_3)_2 \cdot CH_2 \cdot COOC_2H_5,$$

has been prepared in large quantities by the above process, the details of preparation being the following. Sodium (23 grams) is dissolved in alcohol (300 grams), the solution of sodium ethoxide mixed with ethylic cyanacetate (113 grams), ethylic dimethylacrylate (129 grams) is then added, and the whole heated in a reflux apparatus on the water bath. The sodium derivative of ethylic cyanoacetate, which at first separates as a white, crystalline powder, slowly dissolves, and the liquid darkens and gradually sets to an almost solid cake of the sodium derivative of the condensation product, the reaction being finished in about 24 hours. Water is now added, and the oily condensation product extracted with ether in the usual way; the ethereal solution, after washing with water and drying over calcium chloride, deposits a thick oil which, after two distillations under reduced pressure, passes over constantly at 190° (30 mm.), and consists of pure ethylic cyanodimethylglutarate.

0·2614 gave 13·5 c.c. nitrogen at 20° and 750 mm. N = 5·80.

$C_{12}H_{19}NO_4$ requires N = 5·81 per cent.

The yield of this substance produced in the above reaction is about 15 per cent. of the theoretical.

The principal product formed in this condensation is the acid ethylic salt of the substance just mentioned, that is, *ethylic hydrogen α-cyano-ββ-dimethylglutarate*, $COOH \cdot CH(CN) \cdot C(CH_3)_2 \cdot CH_2 \cdot COOC_2H_5$; this is obtained on acidifying the mother liquors of the condensation product mentioned above and extracting with ether. After thoroughly washing the ethereal solution, drying over calcium chloride and evaporating the ether, a thick oil is left, which was not analysed, since, for reasons stated below, it cannot be purified by distillation, and it showed no signs of crystallising. The yield of this substance formed is no less than 60—70 per cent. of the theoretical.

* This immensely increased yield is not confined to this condensation, since it has been found that a similar result is obtained when other unsaturated ethereal salts, such as ethylic crotonate, ethylic methylacrylate, &c., are employed, and the products formed in this way are at present being investigated by one of us.

It is very difficult to understand why this acid ethereal salt should be produced in such large quantities; its formation is certainly not due to the presence of water, as several careful experiments which were made with specially dried alcohol gave, in every case, the same yield.

When distilled under ordinary pressures, this acid ethereal salt is readily decomposed, with elimination of carbon dioxide and formation of *ethylic γ-cyano-ββ-dimethylbutyrate*, $CN\cdot CH_2\cdot C(CH_3)_2\cdot CH_2\cdot COOC_2H_5$, which is a mobile oil distilling without decomposition at 244°.

0·2783 gave 21·8 c.c. of nitrogen at 20° and 735 mm. N = 8·66.

$C_9H_{15}O_2N$ requires N = 8·28 per cent.

When digested with concentrated hydrochloric acid in a reflux apparatus, it rapidly dissolved, and on cooling and mixing with an equal bulk of water, a mass of crystals separated, which, on examination, was found to consist of the imide of dimethylglutaric acid.

ββ-Dimethylglutarimide, $(CH_3)_2C<\begin{matrix}CH_2\cdot CO\\CH_2\cdot CO\end{matrix}>NH$.

This substance is produced by the hydrolysis either of ethylic α-cyanodimethylglutarate or hydrogen ethylic cyanodimethylglutarate, the process in the two cases being somewhat differently conducted. When the first or neutral ethylic salt is employed, the pure substance (60 grams) is heated with methyl alcoholic potash (50 grams) for 2 hours, the solution evaporated until free from alcohol, acidified, and extracted with ether. After evaporating the ether, the residue, which probably consists principally of cyanodimethylglutaric acid, is digested in a reflux apparatus with concentrated hydrochloric acid for 3 hours, when, on evaporating, the whole becomes filled with colourless needles of the imide; these are collected with the aid of the pump and recrystallised from water. In the case of the hydrogen ethylic salt, it is only necessary to boil with an equal volume of concentrated hydrochloric acid for 3 hours, in order to get directly an almost quantitative yield of the imide, care being taken to so moderate the reaction as to avoid loss from the evolution of carbonic anhydride, which is apt to become very vigorous.

ββ-Dimethylglutarimide crystallises from water in long, colourless needles, which melt at 144°, and at a higher temperature distil unchanged. It is very sparingly soluble in cold water, readily in hot water, and is almost insoluble in dry ether.

0·3034 gave 26 c.c. nitrogen at 17° and 750 mm. N = 9·82.

$C_7H_{11}NO_2$ requires N = 9·93 per cent.

This imide is quantitatively converted into $\beta\beta$-dimethylglutaric acid (m. p. 101°) on heating in a closed tube with concentrated hydrochloric acid for 5 hours at 200°, or by heating with dilute sulphuric acid (50 per cent.) for 3 hours on a sand bath, the acid being readily obtained from the products of hydrolysis by extraction with ether in the usual way.

$\beta\beta$-Dimethylglutaric Anhydride, $\begin{matrix} CH_2\cdot C(CH_3)_2\cdot CH_2 \\ | \qquad\qquad\quad | \\ CO\text{——}O\text{——}CO \end{matrix}$.

This anhydride has already been obtained from the acid by treatment with acetic anhydride (Trans., 1896, **69**, 1475), but the process used in the production of the acid and conversion of this into the anhydride has subsequently been much improved, and very large quantities have been prepared for the purposes of this research by the following method. Ethylic cyanodimethylglutarate, as well as the acid ethylic salt, which is always the chief product in the condensation of ethylic cyanoacetate with ethylic dimethylacrylate, are boiled with an equal volume of 50 per cent. sulphuric acid for 12 hours on the sand bath. The exact end point of the reaction is difficult to determine, owing to the fact that the sulphuric acid converts a large proportion of the dimethylglutaric acid into anhydride, and this, like the unhydrolysed ethylic salts, floats on the surface of the aqueous liquid as an oil; we found, however, that 12 hours was sufficient to ensure complete hydrolysis.

The product, when cold, is extracted several times with ether, the ether distilled off, and the residue, without further purification, mixed in the same flask with an equal bulk of acetic anhydride, and boiled for 3 hours on a sand bath, using a reflux condenser. After distilling off most of the acetic anhydride under the ordinary pressure, the crude dimethylglutaric anhydride which remains is purified by fractionation under reduced pressure, when almost the whole passes over at 181° (25 mm.) as a colourless oil, which, on cooling, solidifies to a hard, crystalline cake.

The yield of pure anhydride obtained in this way was over 90 per cent. of theory calculated from the ethylic cyanodimethylglutarate, or about 73 per cent. calculated from the ethylic cyanoacetate originally used in the condensation.

Action of Bromine on Dimethylglutaric Anhydride.—In investigating this reaction, dimethylglutaric anhydride was treated with phosphorus pentabromide and bromine, and the bromo- or dibromo-acid bromides thus produced were converted into methylic or ethylic salts by the action of methylic or ethylic alcohols.

Ethylic α-bromo-$\beta\beta$-dimethylglutarate,

$$COOC_2H_5\cdot CHBr\cdot C(CH_3)_2\cdot CH_2\cdot COOC_2H_5,$$

was prepared from dimethylglutaric anhydride (13 grams) by mixing it with phosphorus pentabromide (50 grams), and heating the mixture in a reflux apparatus on the water bath until the reaction was complete; bromine (16 grams) was then gradually added, and as soon as the vigorous evolution of hydrogen bromide had ceased the whole was heated on the water bath until colourless, and the product poured into well-cooled absolute alcohol. After being allowed to stand for some hours, water was added, when a heavy oil was precipitated which was extracted with ether, and the ethereal solution, after washing well with sodium carbonate solution, was dried over calcium chloride and evaporated. The nearly colourless heavy oil thus obtained, on fractionation, distilled constantly at 181° (20 mm.), and consisted of pure ethylic bromodimethylglutarate.

0·1820 gave 0·0669 AgBr. Br = 27·23.

$C_{11}H_{19}BrO_4$ requires Br = 27·11 per cent.

Hydrogen Ethylic Salt of α-Bromo-ββ-dimethylglutaric Acid,

$COOH \cdot CHBr \cdot C(CH_3)_2 \cdot CH_2 \cdot COOC_2H_5$.

This is precipitated in considerable quantity when hydrochloric acid is added to the sodium carbonate washings obtained as explained in the last paragraph. It is a heavy, colourless oil which distils without decomposition at 240° (35 mm.).

0·1932 gave 0·0771 AgBr. Br = 29·80.

$C_9H_{15}BrO_4$ requires Br = 29·97 per cent.

The formation of this acid ethylic salt in the proportion of about 20 per cent. of the total product of bromination is not due to the presence of water in the alcohol used, as is shown by the fact that exactly the same amount was formed in an experiment in which extra precautions were taken to eliminate, as far as possible, every trace of water. It seems to us probable that, from the examination of a number of similar cases, some acid bromides have the power of decomposing alcohol in such a way as to form the free acid and ethylic bromide, thus: $R \cdot COBr + HO \cdot C_2H_5 = R \cdot COOH + C_2H_5Br$.

It is also possible that the position of the bromine atom may account for the difficulty with which this hydrogen ethylic salt is further etherified, as an experiment which we made with the object of converting the hydrogen ethylic salt into the neutral ethereal salt, by means of alcohol and hydrogen chloride, showed that very little etherification had taken place.

Methylic α-bromo-ββ-dimethylglutarate,

$COOCH_3 \cdot CHBr \cdot C(CH_3)_2 \cdot CH_2 \cdot COOCH_3$,

is obtained when the bromo-acid bromide of dimethylglutaric acid,

prepared as explained above, is poured into well cooled methylic alcohol. It is a mobile liquid boiling at 172° (20 mm.).

Lactone of α-Hydroxy-ββ-dimethylglutaric Acid,

$$\begin{array}{l} COOH\cdot CH\cdot C(CH_3)_2\cdot CH_2 \\ \quad\quad O\text{——————}CO \end{array}$$

This interesting substance, which is isomeric with the caronic acids, was prepared as follows.

The hydrogen ethylic salt of bromodimethylglutaric acid (20 grams) was dissolved in dilute sodium carbonate and boiled in a reflux apparatus on a sand bath, care being taken that the solution always had a distinctly alkaline reaction. As soon as a small quantity of the liquid gave no precipitate with hydrochloric acid, the whole was acidified, saturated with ammonium sulphate, and repeatedly extracted with ether; the dried ethereal solution, when evaporated, gave a hard, crystalline mass which, on being left in contact with porous porcelain for some days, became quite colourless and melted at 80—100°. In order to purify this crude product, and especially with the object of determining whether it contained any *trans*-caronic acid (p. 59), the lactone was dissolved in a slight excess of ammonia, evaporated on the water bath, and the well dried ammonium salt warmed with absolute alcohol, when the whole dissolved readily, showing that no *trans*-caronic acid was present. Ether was then added to the alcoholic solution until a slight turbidity was produced, and the fine, transparent prisms of the pure ammonium salt deposited on standing were collected, washed, and converted into the acid, which was further purified by repeated recrystallisation first from benzene and then from water. Analysis.

0·1643 gave 0·3225 CO_2 and 0·0932 H_2O. C = 53·53; H = 6·30.
$C_7H_{10}O_4$ requires C = 53·16; H = 6·33 per cent.

This lactone melts at 112°, and when heated in a small retort distils without change. It is readily soluble in ether, acetone, ethylic acetate, and hot benzene, moderately in chloroform, and almost insoluble in light petroleum.

Action of Alcoholic Potash on Ethylic α-Bromo-ββ-dimethylglutarate. Formation of cis- *and* trans-*Caronic Acids.*

$$\begin{array}{l} \quad\quad C(CH_3)_2 \\ \quad\quad\quad\diagup\quad\diagdown \\ COOH\cdot CH\text{—}CH\cdot COOH. \end{array}$$

In this interesting experiment, the brom-ethereal salt (15 grams) was digested in alcoholic solution with caustic potash (15 grams) for

10 hours, and the product, after being freed from alcohol by evaporation on the water bath with the addition of water, was dissolved in water, acidified, and extracted several times with ether. On distilling off the ether, a syrupy mass was obtained, which became partially solid on standing; this was dissolved in a little water and saturated with hydrogen chloride, when the crystalline solid, which slowly separated after being collected and dried on a porous plate, melted indefinitely between 170° and 200°. This crude substance was dissolved in ammonia, evaporated to dryness, and the residual solid ammonium salt ground up with cold absolute alcohol; a small quantity passed into solution, but most of it remained undissolved.* The insoluble salt was collected, washed with absolute alcohol, dissolved in a little water, acidified and extracted with ether; the ethereal solution, on evaporating, deposited a solid acid which even before recrystallising melted at 210—212°, and after recrystallising from water at 213°. This substance is trans-*caronic acid.* The alcoholic filtrate from the insoluble ammonium salt of *trans*-caronic acid, on being mixed with ether and allowed to stand, deposited a small quantity of crystalline solid; this, after collecting, acidifying, and extracting with ether, yielded an acid melting at 176°, which, doubtless, consisted of *cis*-caronic acid (m. p. 176°), but the quantity was too small for analysis. In this hydrolysis, therefore, both the caronic acids appear to be formed, but the *trans*-modification in far larger quantity than the *cis*-modification.

On evaporating the solution after the precipitation of the *cis*- and *trans*-caronic acids to dryness with ammonia, and dissolving the residue in alcohol, an oily ammonium salt was precipitated on the addition of much ether, which, on long standing, became solid; from this, on acidifying, a considerable quantity of the lactone of hydroxydimethylglutaric acid was obtained, melting at 112°.

Action of Potash on the Hydrogen Ethylic Salt of α-Bromo-ββ-dimethylglutaric Acid.

This hydrolysis, which gives by far the best yield of *trans*-caronic acid, was conducted as follows. Equal weights of the brom-ethereal salt and caustic potash were heated together in alcoholic solution in a reflux apparatus for 3 hours, and after evaporating the alcohol, acidifying, and extracting with ether, exactly as explained in the last experiment, a hard, solid, crystalline cake was obtained; this, on being crystallised once from water, melted at 213°, and consisted of pure *trans*-caronic acid. On treating this acid and its mother liquors

* This salt is the acid ammonium salt of *trans*-caronic acid, and has the formula $C_7H_{13}NO_4$ (Baeyer, *Ber.*, 1896, **29**, 2800).

with ammonia and alcohol, as explained above, we were not able to extract even traces of the *cis*-modification or of the lactone of hydroxydimethylglutaric acid.

It is remarkable that hydrogen ethylic bromodimethylglutarate should behave so differently from the normal ethylic salt on treatment with potash under the same conditions, and that in the latter case, besides *trans*-caronic acid and traces of the *cis*-modification, such considerable quantities of the lactone of hydroxydimethylglutaric acid should be produced.

The formation of *trans*-caronic acid from the hydrogen ethylic salt seems to us to prove that this salt has the formula

$$COOH\cdot CHBr\cdot C(CH_3)_2\cdot CH_2\cdot COOC_2H_5,$$

given to it on p. 50, and that elimination of hydrogen bromide takes place before hydrolysis. If this ethereal salt had the alternative formula, $COOC_2H_5\cdot CHBr\cdot C(CH_3)_2\cdot CH_2\cdot COOH$, the elimination of hydrogen bromide would be expected to take place between the bromine atom and the hydrogen atom of the carboxyl group, and the lactone of hydroxydimethylglutaric acid would be formed; this, however, is not the case.

Action of Diethylaniline on Ethylic Bromodimethylglutarate.—As it has frequently been found that diethylaniline is a very valuable reagent for removing hydrogen bromide from organic substances, it was thought that interesting results might be obtained if its behaviour were investigated in the present instance. Accordingly, 50 grams of ethylic bromodimethylglutarate was boiled in a reflux apparatus with 75 grams of pure diethylaniline for 2 hours, and after cooling, the nearly solid product was treated with dilute hydrochloric acid, and the oil which separated extracted with ether. The ethereal solution was dried, evaporated, and the residual oil fractionated a great many times, first under reduced and then under the ordinary pressure. It was thus separated into two fractions which boiled at 241° and at about 265—275°.

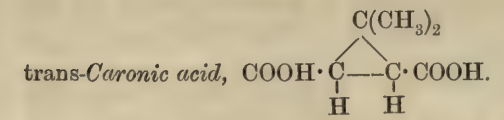
The oil boiling at 241°, on analysis, gave the following numbers.

0·1345 gave 0·3032 CO_2 and 0·1087 H_2O. C = 61·48; H = 8·98.

$C_{11}H_{18}O_4$ requires C = 61·68; H = 8·41 per cent.

Since this oil, on hydrolysis, yielded *trans*-caronic acid, it is evidently the ethereal salt of this acid.

The fraction 265—275°, which was not analysed, gave, on hydrolysis, the lactone of hydroxydimethylglutaric acid, and is evidently the ethereal salt of this lactonic acid. These two substances were obtained in about equal quantities.



trans-*Caronic acid*, $COOH \cdot \underset{H}{C}\!\!<\!\!\begin{matrix}C(CH_3)_2\\ \\ \end{matrix}\!\!>\!\!\underset{H}{C} \cdot COOH$.

The synthetical acid has properties identical with those described by Baeyer and Villiger (*Ber.*, 1896, **29**, 2800) as characteristic for the acid from carone. It is sparingly soluble in cold water, but readily in hot water, and separates from its hot solution in prisms which melt at 213°. It is very sparingly soluble in ether, benzene, and cold water, and almost insoluble in chloroform and light petroleum.

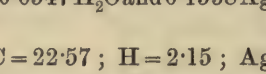
0·1504 gave 0·2913 CO_2 and 0·0888 H_2O. C = 52·82 ; H = 6·56.
$C_7H_{10}O_4$ requires C = 53·16 ; H = 6·33 per cent.

The *silver salt* is precipitated as a white, crystalline powder when silver nitrate is added to a neutral solution of the ammonium salt.

0·2660 gave 0·2177 CO_2, 0·0547 H_2O and 0·1538 Ag. C = 22·33; H = 2·29; Ag = 57·82.
$C_7H_8O_4Ag_2$ requires C = 22·57 ; H = 2·15 ; Ag = 58·06 per cent.

trans-Caronic acid does not give an anhydride when digested with acetic anhydride, but when heated with acetic anhydride at 220° it yields the anhydride of *cis*-caronic acid (p. 61). That it is a saturated acid is shown by the fact that its solution in sodium carbonate does not reduce permanganate.

Conversion of trans-*Caronic Acid into Terebic Acid*,



$\begin{matrix}O\text{———}C(CH_3)_2\\ CO \cdot CH_2 \cdot CH \cdot COOH\end{matrix}$

It was stated in the introduction to this paper that one of the most remarkable reactions of *trans*- and *cis*-caronic acid discovered by Baeyer, was the transformation of these acids into terebic acid by the action of hydrobromic acid at 100°, and it was consequently of importance to show that the synthetical acids behaved in the same manner under the same conditions.

About 0·5 gram of pure synthetical *trans*-caronic acid was heated with about 5 c.c. of concentrated hydrobromic acid (saturated at 0°) for 5 hours at 100° ; the hydrobromic acid was then removed by evaporation on the water-bath, and the residue recrystallised from water ; the colourless, cubic crystals melting at 174° thus obtained gave the following numbers on analysis.

0·1422 gave 0·2757 CO_3 and 0·0802 H_2O. C = 52·87 ; H = 6·26.
$C_7H_{10}O_4$ requires C = 53·16 ; H = 6·33 per cent.

Terebic acid has the same empirical formula and the same melting point as *cis*-caronic acid, but in other respects these acids possess very different properties, and there can be no doubt that the acid obtained in the above experiment was terebic acid, and not unchanged *cis*-caronic acid, for the following reasons (compare Baeyer, *Ber.*, 1896, 29, 2799). This acid yields an ammonium salt which differs from the ammonium salt of *cis*-caronic acid in that, besides having a different crystalline form, its solution in alcohol is not precipitated by ether. It gives, with silver oxide, a silver salt which is readily soluble in water and crystallises in needles, and on boiling with baryta water it yields the characteristic crystalline barium salt of diaterebic acid. Finally, a small quantity heated in a test tube gave the odour of pyroterebic acid,

$$\begin{matrix} O\text{——}C(CH_3)_2 \\ | \quad\quad | \\ CO\cdot CH_2\cdot CH\cdot COOH \end{matrix} = COOH\cdot CH_2\cdot CH{:}C(CH_3)_2 + CO_2,$$

and the residue, dissolved in soda, instantly reduced permanganate, a behaviour not shown by *cis*-caronic acid, which, under these conditions, is simply converted into its anhydride.

Conversion of trans-*Caronic Acid into* cis-*Caronic Acid.*

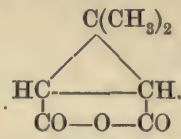
This conversion, which had not previously been observed, may be readily accomplished in the following way. *trans*-Caronic acid is mixed with three times its weight of freshly distilled acetic anhydride, and the mixture heated in a sealed tube for 6 hours at 220°. The dark brown product is then freed from the excess of acetic anhydride by distillation, the residue dissolved in boiling water, digested with animal charcoal, filtered, and evaporated to a small bulk; on cooling, large, glistening, colourless crystals separate, which melt at 176°, and consist of pure *cis*-caronic acid.

0·1602 gave 0·3108 CO_2 and 0·0900 H_2O. C = 52·91; H = 6·24.
$C_7H_{10}O_4$ requires C = 53·16; H = 6·33 per cent.

cis-Caronic acid, $\begin{matrix} & C(CH_3)_2 & \\ & \diagup\quad\diagdown & \\ HC & \text{———} & CH \\ | & & | \\ COOH & & COOH \end{matrix}$, is very sparingly soluble in cold water, but readily in hot water, and crystallises from water most beautifully in brilliant, glistening plates with bevelled edges. It is sparingly soluble in dry ether and in light petroleum, and practically insoluble in chloroform; it dissolves readily in sodium carbonate, and this solution does not decolorise permanganate. When heated above its melting point, *cis*-caronic acid is rapidly converted into its

anhydride. The ammonium salt of *cis*-caronic acid is readily obtained by dissolving the acid in excess of aqueous ammonia and evaporating the solution on a water bath. The crystalline residue differs most sharply from the ammonium salt of the *trans*-acid in being readily soluble in absolute alcohol; from its alcoholic solution, it is precipitated by ether in the form of slender needles. When *cis*-caronic acid is heated with hydrobromic acid, under the conditions given in detail in the corresponding experiment with the *trans*-acid (p. 59), it is converted into *terebic acid* melting at 174°.

It will be seen from this short description of the properties of *cis*-caronic acid that the synthetical acid is identical with the acid obtained by Baeyer (*loc. cit.*) from carone.

Anhydride of cis-*Caronic acid*,  —This anhydride is formed either when *cis*-caronic acid is distilled, or when *trans*-caronic acid is heated at 220° with acetic anhydride, but it is best prepared by boiling *cis*-caronic acid with acetyl chloride until hydrochloric acid ceases to be evolved, evaporating, and crystallising the residue from dry ether, when lustrous plates are obtained which melt at 56°.

There can be no doubt that this is the anhydride of the *cis*-acid, because it is, as Baeyer found (*loc. cit.*, p. 2799), quantitatively converted into the acid on boiling with water.

The authors wish to state that this research was carried out with the aid of a grant from the Royal Society Research Fund, and that they are indebted to Mr. F. H. Lees for making most of the analyses given in this and the succeeding communication.

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SYNTHESIS OF $\alpha\beta\beta$-TRIMETHYLGLUTARIC ACID, $COOH{\cdot}CH(CH_3){\cdot}C(CH_3)_2{\cdot}CH_2{\cdot}COOH$.

BY

WILLIAM H. PERKIN, JUN.,

AND

JOCELYN F. THORPE.

From the Transactions of the Chemical Society, 1899.

Synthesis of $\alpha\beta\beta$-Trimethylglutaric Acid, $COOH\cdot CH(CH_3)\cdot C(CH_3)_2\cdot CH_2\cdot COOH$.

By W. H. Perkin, jun., and Jocelyn F. Thorpe.

Of the four theoretically possible trimethylglutaric acids, two only, up to the present, have been prepared synthetically, namely, the aaa_1-acid, $COOH\cdot C(CH_3)_2\cdot CH_2\cdot CH(CH_3)\cdot COOH$, by Auwers and Victor Meyer (*Ber.*, 1890, **23**, 293) from ethylic α-bromisobutyrate and "molecular" silver, and the $aa\beta$-acid, $COOH\cdot C(CH_3)_2\cdot CH(CH_3)\cdot CH_2\cdot COOH$,

which was prepared by us (Trans., 1897, 71, 1187), by the reduction of the corresponding trimethylglutaconic acid,

$$COOH\cdot C(CH_3)_2\cdot C(CH_3){:}CH\cdot COOH.$$

The remaining two acids are

$\alpha\beta\beta$ ..... $COOH\cdot CH(CH_3)\cdot C(CH_3)_2\cdot CH_2\cdot COOH$, and
$\alpha\beta a_1$ ..... $COOH\cdot CH(CH_3)\cdot CH(CH_3)\cdot CH(CH_3)\cdot COOH$.

Of these, the first has a special interest, for the following reason.

By the oxidation of camphoric acid with permanganate at the ordinary temperature, Balbiano (*Ber.*, 1894, **27**, 2133; 1897, **30**, 1908), obtained an acid of the formula $C_8H_{12}O_5$, to which he assigned the constitution

$$COOH\cdot C(CH_3)\cdot C(CH_3)_2\cdot CH\cdot COOH.$$
$$\quad\quad\quad

and elimination of carbon dioxide, but, although tried under very varied conditions, no trace of this acid was obtained.

It was then thought possible that the ethylic trimethylpropanetricarboxylate, $(COOC_2H_5)_2C(CH_3)\cdot C(CH_3)_2\cdot CH_2\cdot COOC_2H_5$, which should have resulted from the above experiment, might be formed by the condensation of ethylic dimethylacrylate with the sodium derivative of ethylic methylmalonate, but the experiments made in this direction did not yield a trace of the desired compound, and many other syntheses, which need not be mentioned here, also gave negative results. Ultimately, we discovered the following synthesis, which is so easily carried out that large quantities of $a\beta\beta$-trimethylglutaric acid can now be obtained in a short space of time.

The method consists in heating together ethylic dimethylacrylate and the sodium derivative of ethylic cyanacetate in alcoholic solution until the condensation to the sodium derivative of *ethylic cyanodimethylglutarate*, which probably has the formula,

$$COOC_2H_5\cdot C(CN)Na\cdot C(CH_3)_2\cdot CH_2\cdot COOC_2H_5,$$

is complete (see p. 52).

The crude product is then directly treated with methylic iodide, when an almost quantitative yield of ethylic cyanotrimethylglutarate, $COOC_2H_5\cdot C(CH_3)(CN)\cdot C(CH_3)_2\cdot CH_2\cdot COOC_2H_5$, is obtained. This, on hydrolysis with methyl alcoholic potash or hydrochloric acid, yields the beautiful, crystalline *imide* of $a\beta\beta$-trimethylglutaric acid,

$$C(CH_3)_2\begin{<}\begin{matrix}CH(CH_3)\cdot CO\\ CH_2\text{——}CO\end{matrix}\end{>}NH,$$

which, when heated with hydrochloric acid, at 200°, is converted quantitatively into $a\beta\beta$-trimethylglutaric acid.

A direct comparison of the acid thus synthesised with that obtained from camphoric acid was rendered possible by the kindness of Professor Balbiano, who sent us a sample of the acid which he was the first to prepare.

Both acids melted at 87°, and on treatment with acetyl chloride yielded the same anhydride melting at 82°, and from this by the action of aniline an anilic acid was prepared which in both cases melted at 150—151°, so that there can be no doubt as to the identity of the synthetical acid and Balbiano's acid.

In experimenting with $a\beta\beta$-trimethylglutaric anhydride, it was found that, not only does it crystallise from water unchanged, but that it actually crystallises with water of crystallisation, in prisms melting at 61°, and without being converted into the acid.

This is certainly a very unusual property of an anhydride, and the only somewhat similar case which we have been able to find is that of the β-lactone of dimethylmalic acid, $\begin{matrix}(CH_3)_2C\text{——}CH\cdot COOH\\ \quad\quad\quad\

as Baeyer and Villiger (*Ber.*, 1897, **30**, 1955) have shown, crystallises with $1H_2O$.

We are at present engaged in investigating other condensations between unsaturated ethereal salts and α-cyano-ethereal salts, and also on the action of halogen compounds on the sodium derivative of ethylic cyanodimethylglutarate, and we are especially interested in the ethereal salt which this sodium derivative yields on treatment with ethylic bromacetate, because, if Baeyer's formula for isocamphoronic acid be correct, this should lead to a synthesis of this very important acid.

Ethylic α-Cyano-α_1-ββ-trimethylglutarate,
$COOC_2H_5 \cdot CH(CN) \cdot C(CH_3)_2 \cdot CH(CH_3) \cdot COOC_2H_5$.

In order to prepare this substance, ethylic dimethylacrylate is digested in alcoholic solution with the sodium derivative of ethylic cyanacetate, as explained on page 52, and after heating for 15 hours excess of methylic iodide is added and the boiling continued until the liquid has a neutral reaction; water is then added, and the oily product extracted with ether. The ethereal solution, after washing well with water, drying over calcium chloride, and evaporating, deposits a thick oil which, after twice fractionating, boils constantly at 181° (25 mm.), and consists of pure ethylic cyanotrimethylglutarate.

0·22 gave 11·8 c.c. nitrogen at 23° and 750 mm. N = 5·94.
$C_{13}H_{21}NO_4$ requires N = 5·50 per cent.

The yield of this pure ethereal salt obtained in this condensation is about 68 per cent. of the theoretical, and it is remarkable that, in this case, only traces of an acid ethereal salt are formed, whereas, as explained on p. 52, if the condensation is worked up before the treatment with methylic iodide the principal product is the acid ethereal salt.

αββ-Trimethylglutarimide, $C(CH_3)_2 \begin{cases} CH(CH_3) \cdot CO \\ CH_2 \text{——} CO \end{cases} NH$.

This substance is formed when ethylic cyanotrimethylglutarate is hydrolysed either with methyl alcoholic potash or with concentrated hydrochloric acid; in the former case, the product often consists of the acid amide, a white, deliquescent solid which, however, can readily be converted into the imide by boiling for a short time with concentrated hydrochloric acid. αββ-Trimethylglutarimide is sparingly soluble in cold, but readily in hot water, and crystallises in long needles closely resembling ββ-dimethylglutarimide (p. 53) in appearance. It melts at 126°.

0·1163 gave 9·4 c.c. nitrogen at 22° and 765 mm. N = 9·20.
$C_8H_{13}NO_2$ requires N = 9·03 per cent.

Silver salt, $C(CH_3)_2<\begin{matrix}CH(CH_3)\cdot CO\\ CH_2CO\end{matrix}>NAg$.—This interesting salt is obtained as a beautiful, crystalline precipitate when dilute ammonia is carefully added to a warm solution of the imide and silver nitrate.

0·0874 gave 0·0363 Ag. Ag = 41·53.
$C_8H_{12}O_2NAg$ requires Ag = 41·22 per cent.

aββ-Trimethylglutaric acid, $COOH\cdot CH(CH_3)\cdot C(CH_3)_2\cdot CH_2\cdot COOH$.

This acid is best prepared from the imide just described by heating it with three times its weight of concentrated hydrochloric acid in a sealed tube for 5 hours at 200°. The product is evaporated to dryness on the water bath, and the residue extracted with ether; after drying over calcium chloride, the ethereal solution deposits the acid in an almost pure condition on evaporation. For the analysis, the acid was crystallised from water, from which it separates in glistening plates melting at 88°.

0·1316 gave 0·2675 CO_2 and 0·0960 H_2O. C = 55·43; H = 8·23.
$C_8H_{14}O_4$ requires C = 55·17; H = 8·05 per cent.

aββ-Trimethylglutaric Anhydride, $\begin{matrix}CH(CH_3)\cdot C(CH_3)_2\cdot CH_2\\ CO\text{———}O\text{———}CO\end{matrix}$.—This, which is the most characteristic derivative of *aββ*-trimethylglutaric acid, is readily prepared by digesting the pure acid for a short time with excess of acetyl chloride, and then evaporating to dryness on the water bath. The crystalline residue, which consists of the almost pure anhydride, crystallises from a mixture of ethylic acetate and light petroleum in prisms which melt at 82°.

0·1445 gave 0·3248 CO_2 and 0·0991 H_2O. C = 61·34; H = 7·62.
$C_8H_{12}O_3$ requires C = 61·54; H = 7·67 per cent.

This anhydride is quite insoluble in cold dilute sodium carbonate solution, and is only very slowly converted into the acid even on boiling.

If this anhydride is boiled with a large quantity of water, and the clear solution, rapidly poured off from the oily drops, is allowed to cool, a small quantity of the anhydride crystallises out in needles (I); the same substance is produced on melting the anhydride under hot water and stirring vigorously until it becomes solid (II). The product in both cases melts at 61°, and consists of the anhydride with half a molecule of water of crystallisation. The following are the results of the analyses of specimens of I and II.

I. 0·2322 gram, after drying on a porous plate for 3 hours, lost 0·0134 gram at 50°. $H_2O = 5·8$ per cent.

II. 0·4712, heated at 50° until constant, lost 0·0242. $H_2O = 5·15$.

$C_8H_{12}O_3 + \frac{1}{2}H_2O$ requires $H_2O = 5·4$ per cent.

The water of crystallisation is given off rapidly on gently warming, and slowly over sulphuric acid in a vacuum desiccator; the residue then melts at 82°, the melting point of the dry anhydride.

$a\beta\beta$-Trimethylglutaranilic Acid,

$$C_6H_5·NH·CO·CH(CH_3)·C(CH_3)_2·CH_2·COOH(?).$$

On the addition of aniline to a solution of the anhydride in benzene, this compound separates after some time as a white, crystalline precipitate. After being purified by recrystallisation from dilute methylic alcohol, from which it separates in long needles, it melted at 150—151°, and, on analysis, gave the following result.

0·2515 gave 12·2 c.c. nitrogen at 21° and 752 mm. $N = 5·47$.

$C_{14}H_{19}NO_3$ requires $N = 5·60$ per cent.

Our thanks are due to Messrs. F. Howles and F. H. Lees, for much valuable help in connection with this and the preceding research, and we wish also to state that the very considerable expense which these experiments have entailed has been largely met by grants from the Royal Society Research Fund.

OWENS COLLEGE,
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RICHARD CLAY AND SONS, LIMITED, LONDON AND BUNGAY

EXPERIMENTS ON THE CONSTITUTION OF ISO-CAMPHORONIC ACID.

BY

WILLIAM HENRY PERKIN, JUN.,

AND

JOCELYN FIELD THORPE.

From the Transactions of the Chemical Society, 1899.

Experiments on the Constitution of Isocamphoronic Acid.

By William Henry Perkin, jun., and Jocelyn Field Thorpe.

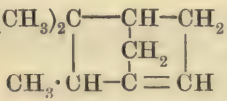
Isocamphoronic acid, $C_9H_{14}O_6$, appears to have first been described by Kachler in 1878 (*Annalen*, **191**, 149), who prepared it, in the first instance, by the oxidation of camphor with nitric acid, and named it hydroxycamphoronic acid.

In 1879, Ballo (*Ber.*, **12**, 1597) oxidised camphor with chromic acid and obtained an acid which he believed to be adipic acid, but this Kachler soon afterwards (*Ber.*, 1880, **13**, 487) showed to be identical with his hydroxycamphoronic acid.

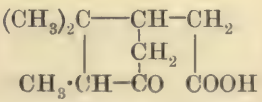
At a later date, Kachler (*Monatsh.*, 1883, **4**, 648) found that considerable quantities of the same acid are produced when "oxycamphor" is oxidised with nitric acid.

The next important contributions to the subject were published by Tiemann (*Ber.*, 1895, **28**, 1344; 1896, **29**, 2613) who showed that isocamphoronic acid is formed from pinonic acid—a product of the oxidation of pinene—and also from α-campholenic acid—an acid closely allied to, and which may easily be converted into, pinonic acid—by oxidation with chromic acid mixture, isoketocamphoric acid being an intermediate product.

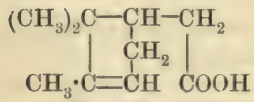
Tiemann is of opinion that the constitutions of these various substances may be represented by the formulæ,



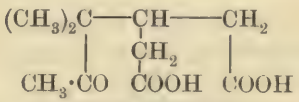
Pinene.



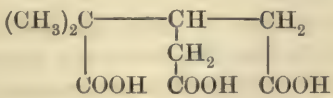
Pinonic acid.



α-Campholenic acid.



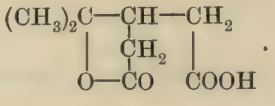
Isoketocamphoric acid.



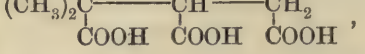
Isocamphoronic acid.

and considers this view of the constitution of isocamphoronic acid is proved, because this acid when heated with concentrated sulphuric acid

at 100°, is decomposed, with evolution of carbonic oxide and formation of terpenylic acid,

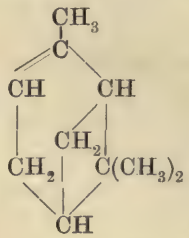


Again, isocamphoronic acid, on oxidation, yields dimethyltricarballylic acid,



the formation of which is readily understood if Tiemann's formula is assumed to be correct.

Baeyer, on the other hand, as the result of his researches on the constitution of pinene, comes to quite different conclusions with regard to the formulæ of this terpene and of its principal decomposition products. Assuming that Wagner's formula for pinene is correct,



he formulates the constitutions of pinonic acid, isoketocamphoric acid, and isocamphoronic acid thus:

Pinonic acid, $CH_3 \cdot CO \cdot CH\langle \begin{matrix} C(CH_3)_2 \\ CH_2 \end{matrix} \rangle CH \cdot CH_2 \cdot COOH$,

Isoketocamphoric acid, $CH_3 \cdot CO \cdot CH_2 \cdot C(CH_3)_2 \cdot CH(COOH) \cdot CH_2 \cdot COOH$.

Isocamphoronic acid, $COOH \cdot CH_2 \cdot C(CH_3)_2 \cdot CH(COOH) \cdot CH_2 \cdot COOH$.

Baeyer explains the formation of the two latter acids from pinonic acid by assuming that an intermediate substance,

$$CH_3 \cdot CO \cdot CH\langle \begin{matrix} C(CH_3)_2 \\ CO \end{matrix} \rangle CH \cdot CH_2 \cdot COOH,$$

is first produced, which then, by hydrolysis, yields isoketocamphoric acid, and he is of opinion that the formation of terpenylic acid from isocamphoronic acid by heating with concentrated sulphuric acid at 100° cannot be taken as a proof of the correctness of Tiemann's formula for the latter acid, since such energetic treatment may have brought about intramolecular rearrangement.

From this short sketch, it will be seen that the determination of the constitution of isocamphoronic acid is a matter of great importance owing to its bearing on the constitution, not only of pinene, but also of camphor, and on this account we have been experimenting, during the last two years, with a view of preparing synthetically an acid of the formula suggested by Baeyer, but the problem is one of unusual difficulty. We have, however, at length obtained an acid which we believe to have this constitution, but which we find is not identical with isocamphoronic acid.

A short time ago (Trans., 1899, **75**, 63), we succeeded in preparing $\alpha\beta\beta$-trimethylglutaric acid by the following series of reactions. Ethylic dimethylacrylate, $(CH_3)_2C{:}CH\cdot COOC_2H_5$, was digested in alcoholic solution with the sodium derivative of ethylic cyanacetate, $CN\cdot CHNa\cdot COOC_2H_5$, when combination took place with formation of the sodium derivative of ethylic cyanodimethylglutarate,

$$COOC_2H_5\cdot C(CN)Na\cdot C(CH_3)_2\cdot CH_2\cdot COOC_2H_5.$$

This, on treatment with methylic iodide, yielded ethylic cyanotrimethylglutarate, $COOC_2H_5\cdot C(CN)(CH_3)\cdot C(CH_3)_2\cdot CH_2\cdot COOC_2H_5$, from which by boiling with dilute sulphuric acid, $\alpha\beta\beta$-trimethylglutaric acid, $COOH\cdot CH(CH_3)\cdot C(CH_3)_2\cdot CH_2\cdot COOH$, was obtained. We now find that, if the sodium derivative of ethylic cyanodimethylglutarate, instead of being treated with methylic iodide, is digested with ethylic bromacetate, the following reaction takes place :

$$COOC_2H_5\cdot C(CN)Na\cdot C(CH_3)_2\cdot CH_2\cdot COOC_2H_5 + BrCH_2\cdot COOC_2H_5 = \begin{matrix} COOC_2H_5\cdot C(CN)\cdot C(CH_3)_2\cdot CH_2 \\ | \qquad\qquad\qquad\quad | \\ CH_2\cdot COOC_2H_5 \quad COOC_2H_5 \end{matrix} + NaBr.$$

The *ethylic cyanodimethylbutanetricarboxylate* thus produced—a colourless oil boiling at 223—227° under 25 mm. pressure—yields, on hydrolysis with dilute sulphuric acid, *dimethylbutanetricarboxylic acid*,

$$\begin{matrix} CH_2 & CH\cdot C(CH_3)_2\cdot CH_2 \\ | & | \qquad\quad | \\ COOH & COOH \qquad COOH \end{matrix}'$$

an acid which, it will be seen, has the same formula as that suggeste by Baeyer for isocamphoronic acid. The synthetical acid obtained by us has the very remarkable property of being apparently incapable of crystallising. When isolated from the product of hydrolysis of ethylic cyanodimethylbutanetricarboxylate by extraction with ether in the usual way, it remains, after evaporating off the ether, as a thick, colourless syrup, which, on standing over sulphuric acid in a vacuum desiccator, froths up owing to the escape of ether, and is converted into a resin very similar to colophony in appearance. As it seemed possible that the acid did not crystallise because it was not quite

pure, a large quantity was reconverted into the triethylic salt, and this, on fractionation, was easily obtained pure as a colourless oil boiling quite constantly at 182—183° under 22 mm., and at 300—302° under 740 mm. pressure, the latter temperature coinciding exactly with the boiling point of the ethylic salt of camphoronic acid.

This ethereal salt, which gave correct numbers on analysis, was carefully hydrolysed, but the acid was again obtained as a resin which showed no signs of crystallising. As the acid yields a calcium salt which is much less soluble in hot than in cold water, a given quantity was separated into five fractions of calcium salts, but these each and all yielded a non-crystallisable acid. Again all attempts to convert the acid into crystalline derivatives, such as the amide, anilide, phenylhydrazide, &c., were unsuccessful. It, however, yields a crystalline strychnine salt, but on decomposing this, the acid was again obtained with the same resinous properties. If the acid is dissolved in acetone, and the solution mixed with benzene and allowed to stand for some weeks, crystals slowly separate which consist of dimethylbutanetricarboxylic acid combined with benzene; these very readily lose benzene, leaving as a residue the same resinous acid. We are therefore forced to the conclusion that this dimethylbutanetricarboxylic acid is incapable of crystallising.

When dimethylbutanetricarboxylic acid is heated in a retort under diminished pressure, it readily loses water, and on distilling the residue, *anhydrodimethylbutanetricarboxylic acid*,

$$\begin{array}{l} CH_2—CH\cdot C(CH_3)_2\cdot CH_2 \\ CO\cdot O\cdot CO \qquad\qquad COOH \end{array}$$

passes over constantly at 240—242° under 16 mm. pressure as a thick oil which shows no sign of crystallising, and which, when treated with aniline, β-naphthylamine, &c., gives only resinous derivatives.

Experiments are in progress with the view of preparing synthetically the acid of the formula which Tiemann assigns to isocamphoronic acid, and it is hoped that in this way the constitution of this important acid may soon be definitely established.

Experimental.

Ethylic Cyanodimethylbutanetricarboxylate,

$$\begin{array}{l} CH_2———C(CN)\cdot C(CH_3)_2\cdot CH_2 \\ COOC_2H_5 \quad COOC_2H_5 \qquad COOC_2H_5 \end{array}.$$

In order to prepare this substance, sodium (5 grams) is dissolved in absolute alcohol (70 grams), the solution mixed with ethylic cyanacetate (25 grams), and ethylic dimethylacrylate (28 grams)

and the whole heated for 2 days in a reflux apparatus on the water-bath. The white, crystalline sodium compound of ethylic cyanacetate which at first separates, gradually dissolves, and in about 4 hours a light brown liquid is formed. At the end of two days, the product has become converted into a hard, brown mass of the sodium compound of ethylic cyanodimethylglutarate,

$$COOC_2H_5 \cdot C(CN)Na \cdot C(CH_3)_2 \cdot CH_2 \cdot COOC_2H_5.$$

To this, after cooling, ethylic bromacetate (40 grams) is added, and the heating continued, when sodium bromide rapidly separates, and after 6 hours the brown sodium compound is entirely decomposed. The product, which should be quite neutral, is mixed with water and extracted with ether; the ethereal solution is washed well with water, dried over calcium chloride and evaporated, and the residual oil, which weighs about 70 grams, submitted to very careful fractional distillation under reduced pressure (25 mm.). In this way, after four or five fractionations, two principal fractions are obtained boiling respectively at 180—200° and 220—230°. The first of these consists of ethylic cyanodimethylglutarate (Trans., 1899, 75, 52), which has escaped interaction with the ethylic bromacetate; the higher fraction yields, on further distillation, a thick, colourless oil, which boils constantly at about 223—227°, under 25 mm. pressure, and consists of *ethylic cyanodimethylbutanetricarboxylate.*

0·1376 gave 0·291 CO_2 and 0·0902 H_2O. C = 57·67; H = 7·28.
0·1530 ,, 0·3258 CO_2 ,, 0·1026 H_2O. C = 58·07; H = 7·45.
0·3208 ,, 13 c.c. nitrogen at 19° and 735 mm. N = 4·50.
$C_{16}H_{25}O_6N$ requires C = 58·71; H = 7·64; N = 4·28 per cent.

The yield of this cyano-ethereal salt from the quantities given above is about 35 grams.

Dimethylbutanetricarboxylic Acid,

$$COOH \cdot CH_2 \cdot CH(COOH) \cdot C(CH_3)_2 \cdot CH_2 \cdot COOH.$$

This acid is readily obtained by the hydrolysis of ethylic cyanodimethylbutanetricarboxylate, as explained in the introduction to this paper. The pure ethereal salt (10 grams) is mixed with 40 per cent. sulphuric acid (about 50 grams) and the whole heated to boiling in a reflux apparatus for two days, when the ethereal salt rapidly passes into solution with evolution of carbon dioxide and alcohol, the latter being allowed to escape by removing the condenser from time to time for a few minutes. The product is saturated with ammonium sulphate and extracted four times with pure ether, when practically the whole of the acid will have passed into the ether, the ease with which this extraction takes place being somewhat remarkable. The ethereal

solution, after drying over calcium chloride and evaporating, deposits a thick, gummy mass, which apparently consists of nearly pure dimethylbutanetricarboxylic acid, but as all attempts to obtain this acid in a crystalline condition were unsuccessful, it was next converted into its ethylic salt and this subjected to very careful purification. The acid (120 grams) was dissolved in absolute alcohol (500 grams), the solution mixed with one-fifth of its volume of concentrated sulphuric acid, and allowed to stand for 2 days. Water was then added and the ethylic salt extracted four times with ether; the ethereal solution was washed well with water and dilute sodium carbonate, dried over anhydrous potassium carbonate and evaporated, when 87 grams of an almost colourless oil remained. On acidifying the sodium carbonate washings and extracting with ether, 64 grams of an acid ethylic salt were obtained, which was again etherified by treatment with alcohol and sulphuric acid.

The combined ethylic salts were then most carefully fractionated under reduced pressure, and after three distillations, about two-thirds of the whole quantity was obtained as a colourless oil, which distilled constantly at 182—183° under a pressure of about 22 mm., and almost without decomposition at 303—305° under the ordinary pressure.

This oil, on analysis, gave numbers agreeing closely with those required for *ethylic dimethylbutanetricarboxylate.*

0·2026 gave 0·4421 CO_2 and 0·1580 H_2O. C = 59·52; H = 8·66.
0·1824 „ 0·399 CO_2 „ 0·1415 H_2O. C = 59·60; H = 8·62.
$C_{15}H_{26}O_6$ requires C = 59·60; H = 8·61 per cent.

Hydrolysis.—It has been stated in the introduction to this paper that the hydrolysis of pure ethylic dimethylbutanetricarboxylate yielded a resinous acid; the experiment was conducted as follows: The pure ethylic salt (5 grams) was boiled with methyl alcoholic potash (5 grams) for 4 hours, when, on standing, a solid potassium salt separated; this was collected, washed with a little methylic alcohol, dissolved in water and evaporated until quite free from alcohol. The solution was acidified, saturated with ammonium sulphate and extracted four times with pure ether; the ethereal solution was then dried over calcium chloride and evaporated, when a resinous acid was obtained which would not crystallise, even when a crystal of isocamphoronic acid (for a quantity of which acid I am indebted to Prof. Baeyer) was stirred up with it. When left in a vacuum desiccator, the acid frothed up and lost the ether remaining in it only with extreme difficulty. The alcoholic mother liquors of the above potassium salt were also mixed with water, evaporated, acidified, and extracted in the same way, and in this case again the acid remained resinous.

Dimethylbutanetricarboxylic acid, on analysis, gave the following numbers:

0·1251 gave 0·2300 CO_2 and 0·0785 H_2O. C = 50·14; H = 6·97.
0·1376 ,, 0·2520 CO_2 ,, 0·0847 H_2O. C = 49·95; H = 6·83.
$C_9H_{14}O_6$ requires C = 49·54; H = 6·42 per cent.

The somewhat high numbers obtained are due to the fact that, owing to the resinous nature of the substance, it was impossible to remove the last traces of ether.

The *silver* salt, $C_9H_{11}O_6Ag_3$, was obtained by adding silver nitrate to a neutral solution of the ammonium salt as a white, amorphous precipitate, which, after well washing and drying, first over sulphuric acid and then at 100°, gave the following results on analysis:

0·251 gave 0·1835 CO_2, 0·0453 H_2O, and 0·1511 Ag. C = 19·79; H = 2·00; Ag = 60·15.
0·5686 gave 0·3427 Ag. Ag = 60·27.
$C_9H_{11}Ag_3O_6$ requires C = 20·04; H = 2·04; Ag = 60·11 per cent.

A neutral solution of the ammonium salt shows the following behaviour with reagents. *Calcium chloride* gives no precipitate in the cold, but on boiling, a white, amorphous salt separates at once; this is readily soluble in cold, but only sparingly so in boiling water. *Barium chloride* and *zinc chloride* give no precipitates, even on boiling. When *copper sulphate* is gradually added to the neutral solution, the pale-green precipitate which first forms, dissolves in the excess of the ammonium salt, but on adding excess of copper sulphate, the copper salt is thrown down as an insoluble precipitate. *Lead acetate* shows a similar behaviour, yielding, with excess of the precipitant, a white, amorphous, insoluble lead salt.

Since the calcium salt is characteristic, being more soluble in cold than in hot water, it seemed possible that, by making use of this peculiarity, we might succeed in obtaining dimethylbutanetricarboxylic acid in a crystalline condition. The acid (20 grams) was therefore dissolved in an excess of ammonia, mixed with a strong solution of calcium chloride, the clear liquid heated to boiling, and when a considerable quantity of the calcium salt had separated, the whole was rapidly filtered by the aid of the pump, using a hot water funnel; the residue was washed with boiling water and spread on a porous plate. By concentrating and boiling the filtrate and repeating the above process, the 20 grams of acid were ultimately converted into 5 fractions of the calcium salt; these were separately dissolved in water, acidified with hydrochloric acid, and the acid extracted with ether in the usual way, but in all cases a resinous acid was obtained which did not show any signs of crystallising.

After experimenting with several other salts, the strychnine salt was at last prepared by adding powdered strychnine to a strong, warm, aqueous solution of the acid, when it was found that large quantities of the base were very readily dissolved. The solution gradually crystallised, and after standing for 3 weeks, the whole had become filled with ill-defined voluminous, nodular crystals; these were collected by the aid of a vacuum pump, rapidly washed with a little water, and spread on a porous plate. The salt was then dissolved in water, and the strychnine precipitated by means of potash; after filtering and acidifying the filtrate, the acid was extracted in the usual way, but in this case also it was again obtained in the form of a resin.

Anhydrodimethylbutanetricarboxylic Acid,

$$\begin{matrix} CH_2 \\ | \\ CO\cdot O\cdot CO \end{matrix} \!\!-\!\! \begin{matrix} CH\cdot C(CH_3)_2\cdot CH_2\cdot COOH. \\ | \\ CO\cdot O\cdot CO \end{matrix}$$

When pure dimethylbutanetricarboxylic acid is heated in a fractionation flask under reduced pressure (16 mm.), the mass at first froths owing to elimination of water, and the residue then distils completely between 235° and 250°; on refractionation almost the whole passes over between 240° and 242° under 16 mm. pressure as a pale yellow, very thick oil, which, on cooling, sets to an almost solid, transparent resin, and consists of pure anhydrodimethylbutanetricarboxylic acid, as the following analysis shows.

0·1992 gave 0·3926 CO_2 and 0·1069 H_2O. C = 53·81; H = 5·96.
$C_9H_{12}O_5$ requires C = 54·0; H = 6·0 per cent.

This anhydro-acid dissolves readily in water, being evidently again converted into the tribasic acid.

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ON *aa*-DIMETHYLGLUTACONIC ACID AND THE SYNTHESIS OF ISOCAMPHORONIC ACID.

BY

W. H. PERKIN, JUN.

From the Transactions of the Chemical Society, 1902. Vol. 81.

XXV.—*On aa-Dimethylglutaconic Acid and the Synthesis of* iso*Camphoronic Acid.*

By W. H. Perkin, jun.

*iso*Camphoronic acid, $C_9H_{14}O_6$, has been obtained by the oxidation of campholenic acid, camphoroxime, and other derivatives of camphor, and it is also one of the products of the oxidation of pinene. For these

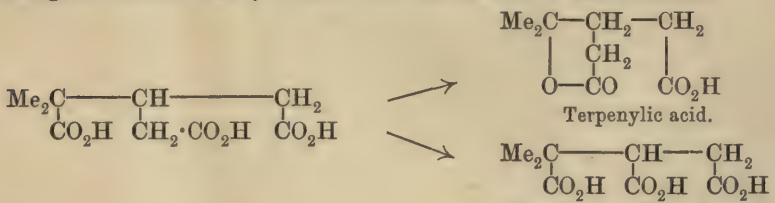
reasons the determination of the constitution of this acid has always been considered to be a matter of great importance, since, until this is definitely proved, it is not possible to obtain a correct view of the relationship which undoubtedly exists between the various members of the camphor and terpene series. For a considerable time, two views as to the constitution of *iso*camphoronic acid have been especially prominent. Baeyer (*Ber.*, 1896, **29**, 2775), as the result of his classical researches on pinene, came to the conclusion that this acid probably had the constitution

$$CO_2H\cdot CH_2\cdot CMe_2\cdot CH(CO_2H)\cdot CH_2\cdot CO_2H,$$

whereas Tiemann (*ibid.*, 2612), who prepared the acid from campholenic acid as well as from pinene, preferred the formula

$$CO_2H\cdot CMe_2\cdot CH(CH_2\cdot CO_2H)_2,$$

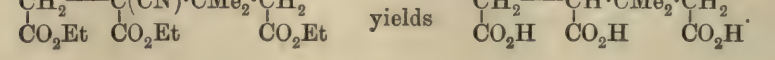
on account of the fact that *iso*camphoronic acid, when treated with concentrated sulphuric acid, is converted into terpenylic acid, and when oxidised with permanganate yields dimethyltricarballylic acid, two changes which are easily understood with the aid of his formula,



but which are difficult to bring in agreement with Baeyer's formula.

In order to decide whether either of these two formulæ represented *iso*camphoronic acid, an experimental investigation on the synthesis of the acids represented by these formulæ has been in progress during the last four years, and in a paper published some time since (Perkin and Thorpe, Trans., 1899, **75**, 897) a method was described by which it was found possible to synthesise the acid having the formula which Baeyer assigned to *iso*camphoronic acid. Briefly stated, this synthesis is as follows:

Ethyl dimethylacrylate, $CMe_2{:}CH\cdot CO_2Et$, is heated with the sodium compound of ethylic cyanoacetate, $CN\cdot CHNa\cdot CO_2Et$, when condensation takes place and the sodium compound of ethyl cyanodimethylglutarate, $CO_2Et\cdot C(CN)Na\cdot CMe_2\cdot CH_2\cdot CO_2Et$, is obtained. When this is heated with ethyl bromoacetate, ethyl cyanodimethylbutanetricarboxylate is produced, and this, on hydrolysis with hydrochloric acid, yields the dimethylbutanetricarboxylic acid, which is the acid represented by Baeyer's *iso*camphoronic acid formula,



The acid thus obtained did not crystallise, and differed from *iso*camphoronic acid in many of its other properties, and it was therefore clearly proved that the latter cannot be a dimethylbutanetricarboxylic acid of this formula. Since these results were obtained, a great number of experiments have been carried out with the object of synthesising the acid having the formula which Tiemann considered must represent *iso*camphoronic acid, but until lately without success.

In the present paper, however, a method is described by which the acid of this formula has been synthesised, and it is shown that the synthetical acid is identical with *iso*camphoronic acid, and therefore Tiemann's view is the correct one, and *iso*camphoronic acid is

$$\begin{array}{ccccc} Me_2C & \text{———} & CH & \text{———} & CH_2 \\ | & & | & & | \\ CO_2H & & CH_2\cdot CO_2H & & CO_2H \end{array}.$$

The synthesis of *iso*camphoronic acid may be briefly described as follows. *aa*-Dimethylglutaric acid, $CO_2H\cdot CMe_2\cdot CH_2\cdot CH_2\cdot CO_2H$, is converted into its anhydride, this is then brominated by treating it with phosphorus pentachloride and bromine, and the product poured into alcohol, when *ethyl* α_1-*bromo-aa-dimethylglutarate* is obtained as an oil boiling at 170° (35 mm.). When this ester is digested with alcoholic potash, decomposition takes place readily, and one of the substances formed is a new *dimethylglutaconic acid*,

$$CO_2H\cdot CMe_2\cdot CH{:}CH\cdot CO_2H,$$

which melts at 172°. If, now, the ester of this acid is digested in alcoholic solution with the sodium compound of cyanoacetic ester, a condensation product is formed which, on hydrolysis with sulphuric acid, yields *iso*camphoronic acid. These changes may be represented thus:

$$CO_2Et\cdot CMe_2\cdot CH{:}CH\cdot CO_2Et + CN\cdot CHNa\cdot CO_2Et =$$

$$\begin{array}{ccc} CMe_2 & \text{——} & CH\cdot CH_2\cdot CO_2Et \\ | & & | \\ CO_2Et & & CNa(CN)\cdot CO_2Et \end{array} = \begin{array}{ccc} CMe_2 & \text{——} & CH\cdot CH_2\cdot CO_2H \\ | & & | \\ CO_2H & & CH_2\cdot CO_2H \end{array}.$$

The acid thus obtained melted at the same temperature as *iso*camphoronic acid, and furthermore a mixture of equal parts of the synthetical acid and of *iso*camphoronic acid from pinene (which Professor von Baeyer kindly sent the author) melted at exactly the same temperature as the constituents. Finally, the synthetical acid, when heated with sulphuric acid, is converted into terpenylic acid with evolution of carbon monoxide, a reaction which, as Tiemann first showed, is highly characteristic of *iso*camphoronic acid. There can therefore be no doubt that the synthetical acid is the same as the *iso*camphoronic acid obtained from camphor and from pinene.

The *aa-dimethylglutaconic acid*, $CO_2H\cdot CMe_2\cdot CH{:}CH\cdot CO_2H$, which

is formed from ethyl α_1-bromo-*aa*-dimethylglutarate by the action of alcoholic potash as described above, is an acid of considerable interest, for the following reasons:

It melts at 172° and is undoubtedly *aa*-dimethylglutaconic acid, since, on oxidation with permanganate, it is quantitatively converted into dimethylmalonic acid and oxalic acid:

$$CO_2H\cdot CMe_2\cdot CH{:}CH\cdot CO_2H + 4O = CO_2H\cdot CMe_2\cdot CO_2H + CO_2H\cdot CO_2H.$$

Two other *aa*-dimethylglutaconic acids have, however, been described, namely, an acid melting at about 133°, which Henrich (*Monatsh.*, 1899, **20**, 559) obtained by heating the sodium compound of glutaconic ester with methyl iodide and then again with sodium and methyl iodide and hydrolysing the product.

I. $CO_2Et\cdot CHNa\cdot CH{:}CH\cdot CO_2Et + MeI =$
$CO_2Et\cdot CHMe\cdot CH{:}CH\cdot CO_2Et + NaI.$

II. $CO_2Et\cdot CNaMe\cdot CH{:}CH\cdot CO_2Et + MeI =$
$CO_2Et\cdot CMe_2\cdot CH{:}CH\cdot CO_2Et + NaI.$

III. $CO_2Et\cdot CMe_2\cdot CH{:}CH\cdot CO_2Et + 2H_2O =$
$CO_2H\cdot CMe_2\cdot CH{:}CH\cdot CO_2H + 2EtOH.$

That this acid melting at about 133° is *aa*-dimethylglutaconic acid is proved by the fact that, on oxidation with permanganate, it also yields dimethylmalonic acid.

Conrad (*Ber.*, 1899, **32**, 137; 1900, **33**, 1921) has prepared a different acid melting at 150°, which he considers to be an *aa*-dimethylglutaconic acid, the process he employed being briefly as follows. Methyl bromodimethylacetoacetate was treated with potassium cyanide and thus converted into methyl cyanodimethylacetoacetate; this, on hydrolysis with acids or alkalis, yields a crystalline substance melting at 214°, which he considers to be the lactone of $\alpha_1\beta$-dihydroxy-*aa*-dimethylglutaric acid. He thinks it probable that the formation of this substance takes place thus:

(*a*) $CN\cdot CH{:}C(OH)\cdot CMe_2\cdot CO_2Me + H_2O$
Methyl cyanodimethylacetoacetate.
$= CN\cdot CH(OH)\cdot CH(OH)\cdot CMe_2\cdot CO_2Me.$

(*b*) $CN\cdot CH(OH)\cdot CH(OH)\cdot CMe_2\cdot CO_2Me + 2H_2O + HCl =$
$CO_2H\cdot CH\cdot CH(OH)\cdot CMe_2$ (O———CO) $+ NH_4Cl + MeOH.$

By heating the lactone with hydriodic acid, he obtained a crystalline lactone melting at 153°, which he concludes is the lactone of hydroxydimethylglutaric acid,

$$CO_2H\cdot CH\cdot CH_2\cdot CMe_2 \quad (O———CO).$$

Lastly, the methyl ester of this lactonic acid, when heated with sodium and *iso*amyl alcohol, undergoes molecular change, yielding an *aa*-dimethylglutaconic acid,

$$CO_2H{\cdot}CH{:}CH{\cdot}CMe_2{\cdot}CO_2H,$$

which melts at 150°. This acid is unsaturated, since its solution in sodium carbonate readily decolorises permanganate, but it is not known whether dimethylmalonic acid is or is not formed during this oxidation. The author of the present paper is, however, of the opinion that this unsaturated acid obtained by Conrad is not *aa*-dimethylglutaconic acid, because the lactone melting at 153° from which it was obtained does not appear to be the lactone of α_1-hydroxy-*aa*-dimethylglutaric acid.

It is shown on p. 259 of this paper that the lactone of this constitution is produced in considerable quantities, along with *aa*-dimethylglutaconic acid, by the action of alcoholic potash on ethylic bromodimethylglutarate.

$$CO_2Et{\cdot}CHBr{\cdot}CH_2{\cdot}\underset{CO_2Et}{CMe_2} \quad \text{gives} \quad CO_2H{\cdot}\underset{O}{CH}{\cdot}CH_2{\cdot}\underset{CO}{CMe_2},$$

and as thus obtained it is a substance which crystallises well from toluene and melts at 83°, or nearly 70° lower than Conrad's lactone. It must be left to further investigation to determine what the constitution of Conrad's unsaturated acid is.

An acid of the formula of *aa*-dimethylglutaconic acid should, of course, exist in *cis*- and *trans*-modifications corresponding with maleic and fumaric acids, and these may be represented thus:

$$CO_2H{\cdot}CMe_2{\cdot}\underset{H{\cdot}C{\cdot}CO_2H}{\overset{\|}{C}}{\cdot}CO_2H \qquad CO_2H{\cdot}CMe_2{\cdot}\underset{CO_2H{\cdot}C{\cdot}H}{\overset{\|}{C}}{\cdot}CO_2H$$

cis. *trans.*

It is probable that the acid melting at 172°, obtained by the hydrolysis of ethyl bromodimethylglutarate, is the *trans*-modification, because of its high melting point, its sparing solubility in water, and the fact that it is not easily attacked by bromine, and does not yield an anhydride on treatment with acetic anhydride. There can also be little doubt that the acid, of melting point about 133°, obtained by Henrich, is *aa*-dimethylglutaconic acid, not only on account of the way in which it is formed, but also because it yields dimethylmalonic acid on oxidation. Possibly this is a mixture of the *cis*- and *trans*-modifications difficult to separate into its constituents by fractional crystallisation, and experiments are at present being made in order to determine whether this is the case.

Many attempts have been made to convert the acid of melting point 172° into the corresponding *cis*-modification, but these have all failed

partly on account of the acid not yielding an anhydride, but principally because the acid is so readily decomposed on heating with elimination of carbon dioxide.

This decomposition seemed so interesting that it was carefully investigated, and it is shown on p. 256 that the elimination of carbon dioxide is accompanied by the formation of an oily, unsaturated acid of the formula $C_6H_{10}O_2$, which boils at 207—208°.

Carbon dioxide may be removed from *aa*-dimethylglutaconic acid, $CO_2H{\cdot}CMe{\cdot}CH{:}CH{\cdot}CO_2H$, in two directions, yielding the following unsaturated acids.

$CO_2H{\cdot}CMe_2{\cdot}CH{:}CH_2$. *Vinyldimethylacetic acid.*

$CHMe_2{\cdot}CH{:}CH{\cdot}CO_2H$. *β*-iso*Propylacrylic acid.*

Since, however, the acid actually obtained is quantitatively converted into a lactone on treating with 33 per cent. sulphuric acid, it cannot be *iso*propylacrylic acid, which contains the double linking in the *αβ*-position. It is therefore *vinyldimethylacetic acid*, and the lactone formed by the action of the sulphuric acid is the *lactone* of *hydroxyethyldimethylacetic acid*, and is isomeric with the *iso*caprolactone which has been obtained by the distillation of terebic acid, $\begin{matrix} Me_2C & \text{---} & CH{\cdot}CO_2H \\ | & & | \\ O{\cdot}CO & \text{---} & CH_2 \end{matrix}$, and in other ways.

$\begin{matrix} CMe_2{\cdot}CH_2{\cdot}CH_2 \\ | \quad\quad | \\ CO \text{---------} O \end{matrix}$

Lactone of hydroxyethyldimethylacetic acid (b. p. 206°).

$\begin{matrix} CMe_2{\cdot}CH_2{\cdot}CH_2 \\ | \quad\quad | \\ O \text{---------} CO \end{matrix}$.

iso*Caprolactone* (b. p. 207°).

The solution of vinyldimethylacetic acid in chloroform instantly decolorises bromine with formation of *dibromoethyldimethylacetic acid*, $CO_2H{\cdot}CMe_2{\cdot}CHBr{\cdot}CH_2Br$, and its unsaturated nature is also shown by the fact that its solution in chloroform instantly reduces permanganate; but, on the other hand, the acid is not acted on by sodium amalgam, a behaviour which has repeatedly been observed in the case of other acids of similar constitution.

Preparation of aa-Dimethylglutaric Anhydride, $\begin{matrix} CMe_2{\cdot}CH_2{\cdot}CH_2 \\ | \quad\quad | \quad\quad | \\ CO \text{---} O \text{---} CO \end{matrix}$.

The method which was employed in preparing the large quantities of this anhydride which were required for the research was as follows.* Finely powdered *iso*lauronolic acid (100 grams) is mixed, in a flask of 1500 c.c. capacity, with 500 c.c. of nitric acid (sp. gr. 1·2) and cautiously heated on the water-bath. As soon as the first violent reaction has

* Compare Blanc (*Bull. Soc. Chim.*, 1898, [iii], **19**, 284).

subsided, the heating is continued for about 6 hours, with a further addition of small quantities of nitric acid of the same strength if it is found that the first quantity is not sufficient to dissolve the *iso*lauronolic acid completely. The clear solution is evaporated to a small bulk, mixed with water, and the evaporation repeated with the constant addition of small quantities of water, until nearly all the nitric acid has been removed. The residue, after concentrating as far as possible, is allowed to stand, when it gradually becomes converted into a semi-solid mass, owing to the separation of dimethylglutaric acid. After the mother liquor * has been removed as far as possible on the pump, the residue is left in contact with porous porcelain until quite dry, and then heated to boiling in a reflux apparatus with twice its weight of acetic anhydride for 6 hours. The acetic acid and excess of anhydride are then distilled off and the crude anhydride purified by fractionation under reduced pressure, when, after two distillations, almost the whole quantity distils at 175—180° (60 mm.), and on cooling sets to a mass of crystals. These are transferred to the pump, and the residue left in contact with porous porcelain; the substance then consists of pure *αα*-dimethylglutaric anhydride melting at 38—40°. On analysis:

0·1371 gave 0·2963 CO_2 and 0·0895 H_2O. C = 59·0; H = 7·3.
$C_7H_{10}O_3$ requires C = 59·1; H = 7·1 per cent.

Ethyl Bromodimethylglutarate, $CO_2Et{\cdot}CMe_2{\cdot}CH_2{\cdot}CHBr{\cdot}CO_2Et$.

In preparing this bromo-ester, dimethylglutaric anhydride (14 grams) is mixed with phosphorus pentachloride (22 grams) in a flask fitted with a ground-in air-tube and the mixture heated to boiling for about 1 hour and until the whole of the pentachloride has dissolved. After cooling, a slight excess of bromine (17 grams) is added and the whole heated on the water-bath for 12 hours. The action of bromine is unusually slow, and it sometimes happens that even after 12 hours the whole of it has not been used up; in such cases, the liquid is sealed up in tubes and heated at 125—130° for 2 hours. The somewhat brownish product is now poured in a thin stream into three times its volume of alcohol, and after the vigorous reaction has subsided, and the whole has become cold, it is poured into a large volume of ice and water. The heavy oil is then extracted twice with ether, the ethereal solution washed with sodium carbonate, dried over calcium chloride, evaporated, and the residual oil rapidly fractionated under reduced pressure, when almost the whole quantity passes over at 165—170°

* A further quantity of crude dimethylglutaric acid may be obtained from this mother liquor by repeatedly evaporating with water and finally allowing the residue to remain over sulphuric acid until nearly solid.

under 35 mm. pressure and consists of nearly pure *ethyl bromodimethylglutarate*. On analysis:

0·217 gave 0·1325 AgBr. Br = 26·1.

$C_{11}H_{19}BrO_4$ requires Br = 27·1 per cent.

Action of Alcoholic Potash on Ethyl Bromodimethylglutarate. Formation of aa-Dimethylglutaconic Acid, $CO_2H{\cdot}CMe_2{\cdot}CH{:}CH{\cdot}CO_2H$.

When the bromo-ester is digested with a large excess of alcoholic potash, hydrolysis and elimination of hydrogen bromide takes place simultaneously with formation of dimethylglutaconic acid and the lactone of hydroxydimethylglutaric acid (p. 259). The process was usually carried out in the following way.

Caustic potash (35 grams) is dissolved in the least quantity of boiling alcohol in a large flask fitted with a wide condenser, and through the top of this the bromo-ester (50 grams) is run in rapidly from a tap funnel, so that the reaction may be as vigorous as possible and yet sufficiently under control to prevent loss through the liquid being forced out of the condenser. The whole is then boiled on the water-bath for 1 hour, diluted with water, and evaporated with successive additions of water until it is quite free from alcohol; the strongly alkaline liquid is then mixed with excess of hydrochloric acid and extracted 10 times with ether.

After washing with water, drying over calcium chloride, and distilling off the bulk of the ether, a point is reached in the concentration when crystals begin to separate; at this stage, the flask is well cooled and shaken, and the crystals collected on the pump and washed with ether.*

The colourless, crystalline mass consists of almost pure *aa-dimethylglutaconic acid*, and after once crystallising from water, needle-shaped crystals were obtained which melted at 172°. On analysis:

0·1740 gave 0·338 CO_2 and 0·1008 H_2O. C = 53·0; H = 6·4.
0·1581 „ 0·308 CO_2 „ 0·0920 H_2O. C = 53·1; H = 6·4.

$C_7H_{10}O_4$ requires C = 53·2; H = 6·3.

aa-Dimethylglutaconic acid melts at 172°, and is very sparingly soluble in cold water, but dissolves readily on boiling. It is readily soluble in methyl alcohol, acetone, or glacial acetic acid, sparingly in chloroform, ether, or toluene; even in boiling toluene it is only dissolved to a very slight extent and in this respect it differs from the *aa*-dimethylglutaconic acid prepared by Henrich (p. 249).

The molecular weight of the acid as determined by the boiling point

* For the description of the treatment of the ethereal mother liquors of these crystals, see p. 259.

method was found to be 146 and 144, whereas the molecular weight of $C_7H_{10}O_4$ is 158. That the acid is a dibasic acid was shown by titration with decinormal caustic soda when 0·1763 gram neutralised 0·044 gram NaOH, whereas this amount of a dibasic acid, $C_7H_{10}O_4$, should neutralise 0·044 gram NaOH.

$\alpha_1\beta$-Dibromo-$\alpha\alpha$-dimethylglutaric Acid, $CO_2H\cdot CMe_2\cdot CHBr\cdot CHBr\cdot CO_2H$,

Dimethylglutaconic acid is not readily attacked by bromine, as is shown by the fact that when suspended in chloroform it does not decolorise bromine, but it may be converted into its dibromo-additive product in the following way. The pure acid is ground to a fine powder and mixed with a large excess of bromine, in which it dissolves; the liquid is left overnight in a closed vessel and then poured on to a watch glass and exposed to the air.

After the bromine has evaporated, an almost colourless residue is obtained which crystallises from glacial formic acid in needles and melts at 217—219°. On analysis:

0·1974 gave 0·231 AgBr. Br = 51·7.

$C_7H_{10}O_4Br_2$ requires Br = 50·3 per cent.

$\alpha_1\beta$-Dibromo-$\alpha\alpha$-dimethylglutaric acid is almost insoluble in cold water, benzene, chloroform, and light petroleum, but dissolves readily in methyl alcohol. When the finely powdered substance is boiled with sufficient water, it rapidly dissolves, much hydrogen bromide is eliminated, and the solution, when concentrated to a small bulk, deposits on cooling beautiful, needle-shaped crystals. These, after recrystallising from water, melt at about 168—170°, the fused mass giving off gas rapidly at 180°, and becoming quite black. The crystals are readily soluble in sodium carbonate in the cold, and the solution does not decolorise permanganate in the cold, but on warming reduction sets in at once. The substance contains much bromine and is evidently the lactone of β-bromo-α_1-hydroxy-$\alpha\alpha$-dimethylglutaric acid,

$$\begin{array}{l} CMe_2\cdot CHBr\cdot CH\cdot CO_2H \\ |\qquad\qquad\quad | \\ CO\text{———}O \end{array}$$

Ethyl Dimethylglutaconate, $CO_2Et\cdot CMe_2\cdot CH{:}CH\cdot CO_2Et$.

In order to prepare this ester, the pure acid was heated in a reflux apparatus with alcohol and sulphuric acid for 6 hours on the water-bath. The product was mixed with water, extracted three times with ether, the ethereal solution washed well with water and dilute sodium carbonate, and after drying over calcium chloride, the ether evaporated

when a colourless oil was obtained which distilled constantly as 195—197° (200 mm.).

0·1679 gave 0·3797 CO_2 and 0·1316 H_2O. C = 61·7; H = 8·7.
$C_{11}H_{18}O_4$ requires C = 61·7; H = 8·4 per cent.

Ethyl dimethylglutaconate is a colourless oil which has a pleasant but pronounced odour closely resembling that of pineapples. It was noticed in its preparation that dimethylglutaconic acid is esterified with great ease, and that only a trace of an acid ester was extracted from the product by means of the sodium carbonate employed.

Oxidation of aa-Dimethylglutaconic Acid. Formation of Dimethylmalonic Acid and Oxalic Acid.

In carrying out this oxidation, pure dimethylglutaconic acid (4 grams) was dissolved in a slight excess of sodium carbonate, water (500 c.c.) was added, and after the solution had been mixed with powdered ice, a cold saturated solution of potassium permanganate was run in until the colour, which disappeared instantaneously at first, remained permanent. During the whole operation, a rapid stream of carbon dioxide was passed, and the liquid was also kept well stirred by means of a turbine. The product was decolorised by adding sodium sulphite, heated to boiling, filtered, and the filtrate and the washings of the manganese precipitate were evaporated to a small bulk. The concentrated residue was acidified and extracted ten times with pure ether and the ethereal solution evaporated, when a syrupy acid was obtained which, on examination, was found to contain much oxalic acid, as well as another acid, evidently dimethylmalonic acid, since, on heating, carbon dioxide was evolved and an oily acid smelling of *iso*butyric acid produced. In order to separate these acids, they were dissolved in water, the solution made strongly alkaline with ammonia, heated to boiling, and then excess of calcium chloride added. After filtering from the calcium oxalate, the filtrate was concentrated and allowed to stand, when a quantity of colourless, star-like crystals separated, which consisted of the calcium salt of dimethylmalonic acid. The crystals were collected, decomposed with hydrochloric acid, and the solution extracted with ether. The ethereal solution was then carefully dried over calcium chloride and evaporated nearly to dryness, when, on standing, glistening, prismatic crystals separated which melted at 190° and consisted of pure *dimethylmalonic acid*:

0·1723 gave 0·2887 CO_2 and 0·0956 H_2O. C = 45·7; H = 6·2.
0·1206 „ 0·2016 CO_2 „ 0·0669 H_2O. C = 45·6; H = 6·1.
$C_5H_8O_4$ requires C = 45·5; H = 6·1 per cent.

As it was most important that there should be no doubt as to the identity of this acid, it was heated in a small retort until the evolution of carbon dioxide had ceased, when an oily acid was produced, which distilled constantly at 154° (748 mm.) and consisted of pure iso*butyric acid*:

0·152 gave 0·3022 CO_2 and 0·125 H_2O. C = 54·2; H = 9·2.
$C_4H_8O_2$ requires C = 54·5; H = 9·1 per cent.

By weighing the calcium oxalate formed, it was found that the dimethylglutaconic acid had been converted almost quantitatively into oxalic and dimethylmalonic acids by oxidation with permanganate under the conditions given above.

Distillation of Dimethylglutaconic Acid. Formation of Vinyldimethylacetic Acid, $CO_2H{\cdot}CMe_2{\cdot}CH{:}CH_2$.

Dimethylglutaconic acid (3 grams) was heated in a small retort by means of a metal-bath, when it first melted, and then, at about 200°, carbon dioxide commenced to come off in quantity. When the evolu- of gas had ceased, the residue, which had a strong odour like that of *iso*valeric acid, was distilled, and nearly the whole quantity passed over at 195—210°, only a small quantity of a thick, dark-coloured oil remaining. The distillate, on cooling, deposited a few crystals, consisting probably of a trace of unchanged acid, but after again distilling, a colourless oil passed over almost constantly at 207—208° (760 mm.), and this showed no signs of crystallising. On analysis:

0·1186 gave 0·2767 CO_2 and 0·0966 H_2O. C = 63·6; H = 9·0.
$C_6H_{10}O_2$ requires C = 63·2; H = 8·8 per cent.

Vinyldimethylacetic acid is a colourless, unpleasant smelling oil, which behaves like an unsaturated acid, since, when dissolved in sodium carbonate, it at once decolorises permanganate at the ordinary temperature; its solution in chloroform also instantly absorbs bromine.

In order to investigate the latter reaction, 1 gram of the acid was dissolved in chloroform, and after cooling in ice water, bromine was added drop by drop until the colour just remained. On exposure to the air in a watch-glass, it was noticed that the liquid gave off a little hydrogen bromide, and after the chloroform had evaporated, a pale yellow oil remained, which when left overnight became semi-solid. In contact with porous porcelain, the dark-coloured mother liquor was rapidly absorbed and a colourless, crystalline mass was left. On analysis:

0·0843 gave 0·1141 AgBr. Br = 60·1.
$C_6H_{10}O_2Br_2$ requires Br = 58·4 per cent.

This substance is evidently *dibromoethyldimethylacetic acid*, $CO_2H\cdot CMe_2\cdot CHBr\cdot CH_2Br$, and in its crude state it melted at about 100°. Unfortunately, the quantity was too small to allow of its being recrystallised. Vinyldimethylacetic acid is apparently not acted on by sodium amalgam, since 1 gram of it, after boiling with excess of sodium amalgam for 1 hour, was recovered unchanged on acidifying and extracting with ether.

Lactone of Hydroxyethyldimethylacetic Acid (*aa-Dimethylbutyrolactone*),

$$\begin{array}{l} CMe_2\cdot CH_2\cdot CH_2 \\ | \qquad\qquad | \\ CO\text{———}O \end{array}.$$

Vinyldimethylacetic acid dissolves in 33 per cent. sulphuric acid, and if the solution is heated to boiling for a few minutes, an oil separates. The product was cooled well, made alkaline by the careful addition of potassium carbonate, and repeatedly extracted with ether. The ethereal solution was dried over potassium carbonate and evaporated, and the residual oil distilled, when almost the whole quantity passed over constantly at 205—206°. On analysis:

0·1568 gave 0·3607 CO_2 and 0·1271 H_2O. C = 62·7; H = 9·0.
$C_6H_{10}O_2$ requires C = 63·2; H = 8·8 per cent.

The *lactone* of *hydroxyethyldimethylacetic acid* has a rather pleasant, fruity odour. It dissolves readily in water, but is reprecipitated on adding potassium carbonate. It is closely related to the lactone of γ-hydroxy*iso*caproic acid (*iso*caprolactone),

$$\begin{array}{l} CMe_2\cdot CH_2\cdot CH_2 \\ | \qquad\qquad | \\ O\text{———}CO \end{array},$$

which boils at 207°, and which Fittig and Bredt (*Annalen*, 1880, 200, 58, 259) first obtained by the distillation of terebic acid, $C_7H_{10}O_4$.

Synthesis of iso*Camphoronic Acid*, $CO_2H\cdot CMe_2\cdot CH(CH_2\cdot CO_2H)_2$.

In carrying out this synthesis, sodium (2 grams) was dissolved in alcohol (30 grams), and the solution of sodium ethoxide thus obtained mixed with ethyl cyanoacetate (13 grams) and allowed to stand for 10 minutes. On adding ethyl dimethylglutaconate (20 grams), it was noticed that there was very little rise of temperature, but the reaction seemed to set in rapidly at 100°, as the sodium compound of ethyl cyanoacetate soon passed into solution and the mass quickly acquired a yellow colour. After heating for 15 hours in a reflux apparatus and allowing to cool, a gelatinous mass was obtained which was mixed with excess of dilute hydrochloric acid and extracted three times with ether. After

washing several times with water and evaporating off the ether, 30 grams of a yellow oil were obtained, which was not fractionated and analysed but at once converted into *iso*camphoronic acid by the following process. The oil is mixed with about twice its volume of 90 per cent. sulphuric acid, in which it dissolves with development of heat but without charring. After standing until cold, the whole is diluted with $1\frac{1}{2}$ vols. of water and heated to boiling in a reflux apparatus for 6 hours, the hydrolysis being facilitated by removing the condenser from time to time in order to allow the alcohol produced to escape. The brownish liquid on standing overnight becomes filled with a mass of crystals and these, after collecting on the pump and washing with a little water, melt at 164° and consist of nearly pure *iso*camphoronic acid. A further considerable quantity in a less pure condition may be obtained from the mother liquors by extraction with ether, evaporating, and leaving the residue, which becomes semi-solid on standing, in contact with porous porcelain.

The crystalline acid obtained in this way was not weighed, but the yield was very considerable, and it is only necessary to recrystallise it once from water in order to obtain it quite pure. On analysis:

0·1821 gave 0·3341 CO_2 and 0·1064 H_2O. C = 50·0; H = 6·5.
0·1651 „ 0·3013 CO_2 „ 0·0972 H_2O. C = 49·7; H = 6·6.
$C_9H_{14}O_6$ requires C = 49·6; H = 6·4 per cent.

The synthetical acid, when rapidly heated, softened at 165° and melted at 168°, whereas the melting point of *iso*camphoronic acid is given as 166°. A sample of pure *iso*camphoronic acid from pinene, which Professor A. von Baeyer was good enough to send the author, was mixed with the synthetical acid without any alteration in the melting point being observable. This, and the fact that the synthetical acid on treatment with sulphuric acid yields terpenylic acid, proves that it is identical with the acid obtained from pinene and camphor.

Conversion of Synthetical iso*Camphoronic Acid into Terpenylic Acid*,

$$Me_2C\text{——}CH\cdot CH_2\cdot CO_2H.$$
$$O\cdot CO\cdot CH_2$$

In carrying out this decomposition, synthetical *iso*camphoronic acid (1 gram) was dissolved in concentrated sulphuric acid (8 grams), and the solution heated at 100°, when bubbles of gas were slowly given off. After 6 hours, the liquid, which had scarcely darkened in colour, was diluted with water and repeatedly extracted with ether, the ethereal solution was washed until free from sulphuric acid, evaporated, and the oily residue mixed with a very little water and allowed to stand. After about 3 days, the crystals which had separated were left

in contact with porous porcelain until dry, and then crystallised from water, when glistening prisms were obtained, which melted at 59—60°, and consisted of hydrated terpenylic acid. On leaving these crystals over sulphuric acid in a vacuum desiccator, they soon became opaque, and after two days the chalky mass melted sharply at 90° and gave the following results on analysis:

0·1634 gave 0·3332 CO_2 and 0·1034 H_2O. C = 55·6; H = 7·0.
$C_8H_{12}O_4$ requires C = 55·8; H = 7·0 per cent.

This acid is therefore terpenylic acid, which, according to Tiemann, crystallises from water in well-defined, hydrated crystals melting at 56°; these, when placed over sulphuric acid in a vacuum desiccator, lose their water of crystallisation, giving a chalky mass which melts at 90°.

Lactone of α_1*-Hydroxy-aa-dimethylglutaric Acid,*

$$\begin{array}{l} CMe_2\cdot CH_2\cdot CH\cdot CO_2H \\ \quad\quad\quad\

glutaconic acid is practically insoluble. After filtering, the filtrate was extracted with ether, the oil obtained after distilling off the ether allowed to solidify, and again treated with hydrochloric acid. Ultimately, the lactone was further purified by recrystallisation from toluene On analysis:

0·1631 gave 0·3177 CO_2 and 0·0950 H_2O. C = 53·1; H = 6·4.
0·1304 „ 0·2544 CO_2 „ 0·0760 H_2O. C = 53·2; H = 6·5.
$C_7H_{10}O_4$ requires C = 53·1; H = 6·3 per cent.

The *lactone* of *α_1-hydroxy-$\alpha\alpha$-dimethylglutaric acid* melts at about 85° but not quite sharply. It is readily soluble in water, and when the crystals are placed on water they rotate rapidly, like camphor crystals, and slowly dissolve. The lactone dissolves readily in hot toluene, but is sparingly soluble in the cold.

That it is a monobasic lactonic acid is shown by its behaviour on titration with decinormal caustic soda solution, when 0·1849 gram, dissolved in cold water, neutralised 0·049 gram NaOH, whereas this amount of a monobasic acid, $C_7H_{10}O_4$, should neutralise 0·047 gram NaOH. A considerable excess of decinormal caustic soda was then added, and the solution heated to boiling for 10 minutes, and the excess of soda estimated by titration with decinormal sulphuric acid. It was then found that the total amount of NaOH taken up was 0·0944 gram, whereas 0·1849 gram of a monobasic lactone acid, $C_7H_{10}O_4$, on dissolving to form the salt of the hydroxy-dibasic acid, should neutralise 0·094 gram NaOH. The first results of titration in the cold show that the lactone ring is hydrolysed only to a very slight extent when the lactonic acid is dissolved in cold water.

The hydroxy-dibasic acid, when set free from its solution in caustic alkali, is obtained on extraction with ether as a colourless syrup, which does not rapidly pass into the lactone, since titration showed that even after standing for a quarter of an hour it consisted principally of the hydroxy-dibasic acid. When, however, the syrup is placed over sulphuric acid in a vacuum desiccator, it is rapidly converted into the lactone and solidifies completely.

Silver Salt of the Lactone of Hydroxydimethylglutaric Acid, $C_7H_9O_4Ag$. —When silver nitrate is added to a neutral solution of the ammonium salt, there is at first no precipitate, but soon the silver salt begins to separate in microscopic needles, and when dried it has the appearance of a silky mass of needles, which are readily soluble in hot, but sparingly in cold, water. On analysis:

0·2310 gave 0·2691 CO_2, 0·0714 H_2O and 0·0941 Ag. C = 31·8; H = 3·4; Ag = 40·7.
$C_7H_9O_4Ag$ requires C = 31·7; H = 3·4; Ag = 40·7 per cent.

The neutral solution of the ammonium salt gives no precipitate with calcium or barium chlorides, or with copper sulphate or lead acetate.

The author wishes to express his thanks to Mr. J. Yates for his valuable assistance in carrying out this investigation, and also to state that some of the expense of the research was met by repeated grants from the Research Fund of the Royal Society.

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RICHARD CLAY AND SONS, LIMITED, LONDON AND BUNGAY

EXPERIMENTS ON THE SYNTHESIS OF CAMPHORIC ACID. PART II.

BY

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AND

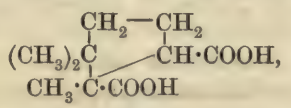
J. L. ROSE.

From the Transactions of the Chemical Society, 1899

Experiments on the Synthesis of Camphoric Acid. Part II.*

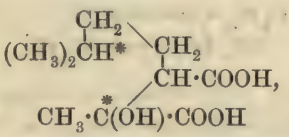
By H. A. Auden, W. H. Perkin, jun., and J. L. Rose.

In 1896, the view was first expressed by one of us (Perkin, Proceedings, 1896, 12, 191) that most of the decompositions of camphoric acid might readily be explained with the aid of the formula

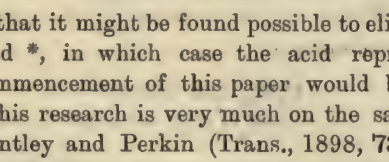


and this formula for camphoric acid was afterwards independently suggested by Bouveault (*Bull. Soc. Chim.*, 1897, [iii], 17, 990), and is now generally known on the continent as "Bouveault's formula." In view of the unusual difficulties which have been found to attend the determination of the constitution of camphoric acid by analytical methods, it was decided some years ago to undertake a long series of experiments with a view of preparing this acid synthetically. The present paper deals with the results which were obtained in an attempt to prepare an acid of the formula given above, and although this result so far has not been realised, our experiments have nevertheless led to the preparation and characterisation of a number of substances of considerable interest which are described in the following pages.

In attempting the synthesis, we proposed in the first place to prepare *$a a_1$-methylisoamyl-a-hydroxysuccinic acid*,



as it was thought that it might be found possible to eliminate water at the points marked *, in which case the acid represented by the formula at the commencement of this paper would be obtained. It will be seen that this research is very much on the same lines as that carried out by Bentley and Perkin (Trans., 1898, 73, 45), who prepared isobutylmethylhydroxyglutaric acid,



* Part I., Trans., 1898, 73, 45.

with a view of removing water at the points *, and of thus obtaining an acid of the formula

$$\begin{array}{l} CH_2\text{———}CH\cdot COOH \\ (CH_3)_2C \qquad\qquad | \\ CH_3\cdot C(COOH)\cdot CH_2 \end{array}$$

which may possibly be camphoric acid.

The latter change could, however, not be brought about, principally on account of the great tendency which the hydroxy-acid shows to pass into a lactone by the elimination of water between the COOH and OH groups situated in the γ-position, a possibility which is not present in the case of the hydroxy-acid which we are considering in this paper. After many unsuccessful attempts, we have ultimately succeeded in preparing *methylisoamylhydroxysuccinic acid* by the following series of reactions. Ethylic isoamylacetoacetate,

$$CH_3\cdot CO\cdot CH(C_5H_{11})\cdot COOC_2H_5,$$

was first caused to combine with hydrogen cyanide by treating its solution in ether at a low temperature with potassium cyanide and hydrochloric acid, and in this way a good yield of *ethylic α-isoamyl-ββ-hydroxycyanobutyrate*, $CH_3\cdot C(OH)(CN)\cdot CH(C_5H_{11})\cdot COOC_2H_5$, was obtained.

When this substance is treated with alcohol and hydrochloric acid, the two most important products are *methylisoamylhydroxysuccinimide*,

$$\begin{array}{l} C_5H_{11}\cdot CH\text{—}CO \\ CH_3\cdot C(OH)\cdot CO \end{array}\!\!>\!NH,$$

a solid, crystalline substance melting at 104°, and an oil which is doubtless ethylic methylisoamylhydroxysuccinate,

$$\begin{array}{l} C_5H_{11}\cdot CH\cdot COOC_2H_5 \\ CH_3\cdot C(OH)\cdot COOC_2H_5 \end{array}.$$

The imide, on boiling with sodium carbonate, yields, in the first place, the corresponding amide, and this is then very slowly further decomposed with elimination of ammonia and formation of the methylisoamylhydroxysuccinic acid,

$$\begin{array}{l} C_5H_{11}\cdot CH\cdot COOH \\ CH_3\cdot C(OH)\cdot COOH \end{array}'$$

which was required for our experiments. This interesting acid crystallises well, melts at 66°, and yields a silver salt of the formula $C_{10}H_{16}Ag_2O_5$, and its method of formation and the study of its properties leave no doubt that it has the constitution assigned to it here. When this acid is distilled, it readily loses water, and an oil passes over at about 260°, which, after careful investigation, has been found

to consist of *methylisoamylmaleic anhydride*, formed according to the equation

$$\begin{matrix} C_5H_{11}\cdot CH\cdot COOH \\ CH_3\cdot C(OH)\cdot COOH \end{matrix} = \begin{matrix} C_5H_{11}\cdot C\cdot CO \\ CH_3\cdot C\cdot CO \end{matrix}\!\!>\!O + 2H_2O,$$

that is to say, the anhydride of an unsaturated acid is formed, and not of the saturated acid containing a ring of five atoms which we had hoped to obtain.

Methylisoamylmaleic anhydride dissolves in potash solution, but on acidifying, the anhydride and not the acid separates, and, in this respect, the substance behaves exactly like xeronic acid,

$$\begin{matrix} C_2H_5\cdot C\cdot COOH \\ C_2H_5\cdot C\cdot COOH' \end{matrix}$$

which, when set free from solutions of its salts, is obtained in the form of its anhydride.

When treated with aniline, methylisoamylmaleic anhydride yields an *anil*, $C_{16}H_{19}NO_2$ (m. p. 70°), and when boiled with hydriodic acid and phosphorus, it is readily reduced, with formation of a mixture of *cis*- and *trans*-methylisoamylsuccinic acids,

$$\begin{matrix} C_5H_{11}\cdot CH\cdot COOH \\ CH_3\cdot CH\cdot COOH' \end{matrix}$$

the former of which melts at 92° and the latter at 142° (compare W. Trevor Lawrence, Proc., 1899, **15**, 163).

In continuation of our experiments, we next investigated the action of reducing agents on ethylic isoamylacetoacetate in order to determine whether the *α-isoamyl-β-hydroxybutyric acid*, $CH_3\cdot CH(OH)\cdot CH(C_5H_{11})\cdot COOH$, which is formed in this way would, on distillation, lose water with formation of a ring compound,

$$\begin{matrix} & CH_2 & \\ (CH_3)_2CH & & CH_2 \\ CH_3\cdot CH(OH) & & CH\cdot COOH \end{matrix} = \begin{matrix} & CH_2 & \\ (CH_3)_2C & & CH_2 \\ CH_3\cdot CH & & CH\cdot COOH, \end{matrix}$$

or whether, as in the case of methylisoamylhydroxysuccinic acid, an unsaturated acid, $CH_3\cdot CH{:}C(C_5H_{11})\cdot COOH$, would be formed.

If the ring compound were formed, the synthesis would be most important, since, on the supposition that the formula for camphoric acid represented at the commencement of this paper is correct, the product would be *dihydroisolauronolic acid* (compare Trans., 1898, **73**, 810).

On investigating the matter, it was found that the hydroxy-acid, on distillation, yields the unsaturated acid, and that apparently no trace of the ring acid is formed in this way.

The *α-isoamylcrotonic acid*, $CH_3\cdot CH{:}C(C_5H_{11})\cdot COOH$, thus obtained

is a colourless oil which distils at 240°, and its constitution is proved by the fact that it yields isobutylacetic acid, $C_4H_9 \cdot CH_2 \cdot COOH$, on oxidation.

Lastly, we investigated the action of hydrogen cyanide on isoamylacetone, $C_5H_{11} \cdot CH_2 \cdot CO \cdot CH_3$, and after hydrolysing the product we obtained in this way small quantities of *α-hydroxy-β-isoamylisobutyric acid*, $C_5H_{11} \cdot CH_2 \cdot C(OH)(CH_3) \cdot COOH$, which melts at 66° and is isomeric with the isoamylhydroxybutyric acid mentioned above. Unfortunately, the yield is scarcely more than 1 per cent. of the theoretical, and therefore we were unable to investigate it as completely as we could have wished.

Preparation and Hydrolysis of Ethylic α-Isoamyl-ββ-hydroxycyanobutyrate, $CH_3 \cdot C(CN)(OH) \cdot CH(C_5H_{11}) \cdot COOC_2H_5$.

In endeavouring to prepare this substance by the addition of hydrogen cyanide to ethylic isoamylacetoacetate, experiments were made under the most varied circumstances, in order to determine the best conditions, and ultimately it was found that the following method, which is very similar to that described by Haller and Held (*Ann. Chim. Phys.*, 1891, [vi], 23, 145), gave the most satisfactory result. Ethylic isoamylacetoacetate (50 grams) is dissolved in ether (50 grams), finely powdered potassium cyanide (25 grams) added, and then the calculated quantity of hydrochloric acid (about 40 c.c. of the ordinary concentrated acid) gradually run in with constant shaking, the temperature being kept below $-10°$ during the whole operation. After standing for 24 hours at the ordinary temperature, the ethereal solution is washed with water, dried over calcium chloride, and the ether distilled off, when a thick, yellow oil is obtained, which consists of crude *ethylic isoamylhydroxycyanobutyrate*, and in this form it was used in all subsequent experiments. The hydrolysis of this crude ethereal salt was carried out by two methods which give different results, namely, (*a*) by means of hydrochloric acid, and (*b*) by means of sulphuric acid.

(*a*) *Hydrolysis by means of Hydrochloric Acid.*—The crude cyanoethereal salt (100 grams) was dissolved in absolute alcohol (150 grams), and the whole saturated with hydrogen chloride, the temperature being kept below 20° by cooling with water. After standing overnight, the product was heated in a reflux apparatus on the water-bath for 2 hours, hydrogen chloride being passed through during the whole time, when large quantities of ammonium chloride separated. The alcoholic solution was poured into water and the oil, which separated, extracted with ether; the ethereal solution was washed with water and very dilute sodium carbonate solution and distilled in steam, in order to remove isoamylacetone, $C_5H_{11} \cdot CH_2 \cdot CO \cdot CH_3$. This substance, which

is always formed, and sometimes in considerable quantity, is evidently produced by the hydrolysis of the unchanged ethylic isoamylacetoacetate present in the crude ethylic isoamylhydroxycyanobutyrate employed in these experiments. The oil remaining in the distillation flask may be treated in two ways: (*a*) it is shaken with dilute ammonia, and the aqueous solution, after filtering from the undissolved oil, is rapidly acidified, when a crystalline precipitate separates, which consists for the most part of *methylisoamylhydroxysuccinimide* (p. 914), or (*b*) the oil is boiled for about an hour with dilute sodium carbonate, when, after filtering and acidifying, a precipitate of *methylisoamylhydroxysuccinamide* is obtained (p. 914). In either case, the oil remaining undissolved, which still contains much nitrogen, is heated in a sealed tube with alcoholic hydrogen chloride for 5 hours at 150°.

After diluting with water and extracting with ether in the usual way, the oil which is obtained on distilling off the ether is fractionated under reduced pressure (20 mm.), and is thus easily separated into three fractions boiling at 60—90°, 120—130°, and 155—175° respectively. The first fraction, on distillation under ordinary conditions, yields a quantity of an oil boiling at 162—163°, and which was found to be *isoamylacetone*.

0·1783 gave 0·4899 CO_2 and 0·2015 H_2O. C = 74·93; H = 12·56.
$C_5H_{11}\cdot CH_2\cdot CO\cdot CH_3$ requires C = 75·0; H = 12·50 per cent.

The second fraction was redistilled, when the greater portion passed over at 120° under 18 mm. pressure, and on analysis was found to consist of ethylic isoamylacetoacetate.

0·2095 gave 0·5049 CO_2 and 0·1863 H_2O. C = 65·73; H = 9·88.
$CH_3\cdot CO\cdot CH(C_5H_{11})\cdot COOC_2H_5$ requires C = 66·0; H = 10·0 per cent.

On repeatedly fractionating the highest fraction, a large quantity of an oil was obtained which boiled remarkably constantly at 163° under 20 mm. pressure, and on analysis gave numbers agreeing fairly well with those required for the ethereal salt of an acid of the same composition as camphoric acid.

0·2173 gave 0·5130 CO_2 and 0·1870 H_2O. C = 64·38; H = 9·56.
0·2029 „ 0·4803 CO_2 „ 0·1726 H_2O. C = 64·55; H = 9·45.
$C_8H_{14}(COOC_2H_5)_2$ requires C = 65·62; H = 9·37 per cent.

It will be shown later that this oil, although boiling so constantly, is a mixture of the ethereal salts of methylisoamylmaleic acid and methylisoamylhydroxysuccinic acid, the latter predominating.

(*b*) *Hydrolysis by means of Sulphuric Acid.*—After a considerable

quantity of ethylic isoamylhydroxycyanobutyrate had been hydrolysed by means of hydrochloric acid, experiments were made with sulphuric acid in the hope that the hydrolysis could, in this way, be completed without the necessity of using sealed tubes, and this was found to be the case. The cyano-ethereal salt (100 grams) was dissolved in alcohol (200 grams), concentrated sulphuric acid (300 grams) was slowly added, and the mixture, after standing for 12 hours, heated for 8 hours on the water-bath; water was then added and the ethereal salt extracted with ether in the usual way. On fractionating the product under reduced pressure, isoamylacetone first passed over, but in less quantity than in the case of the hydrochloric acid hydrolysis; the greater portion of the residue then distilled between 155° and 175° under 20 mm. pressure, and, on examination, was found to have the same composition as the oil of this boiling point obtained in the case of the hydrochloric acid hydrolysis. A small quantity which distilled above 175° deposited, on standing, some crystals of methylisoamylhydroxysuccinimide. If, then, the object is to prepare this imide, the hydrochloric acid hydrolysis should be employed; but if, on the other hand, methylisoamylmaleic anhydride (p. 916) is required, then the sulphuric acid hydrolysis is much to be preferred as being less laborious.

aa_1-Methylisoamyl-a-hydroxysuccinic acid, $\begin{matrix}CH_3\cdot C(OH)\cdot COOH\\ C_5H_{11}\cdot CH\cdot COOH\end{matrix}$.

It was stated in the previous section, that when ethylic isoamylhydroxycyanobutyrate is hydrolysed with alcohol and hydrochloric acid and the product extracted with ammonia, a solid substance separates on acidifying, which, on examination, has been found to be *methylisoamylhydroxysuccinimide*, $\begin{matrix}CH_3\cdot C(OH)\cdot CO\\ C_5H_{11}\cdot CH\text{—}CO\end{matrix}\!>\!NH$. This substance crystallises from light petroleum in colourless needles, melts at 104°, and is readily soluble in alcohol, ether, and benzene, but only sparingly so in cold, light petroleum and water. When heated in small quantities, it distils, apparently without decomposition.

0·1631 gave 0·3610 CO_2 and 0·1280 H_2O. C = 60·36; H = 8·72.
0·2482 ,, 14·65 c.c. nitrogen at 20° and 766 mm. N = 6·88.
$C_{10}H_{17}NO_3$ requires C = 60·30; H = 8·54; N = 7·04 per cent.

When methylisoamylhydroxysuccinimide is boiled with sodium carbonate solution, it gradually dissolves and, on acidifying, the corresponding *methylisoamylhydroxysuccinamide* is obtained as a white, sparingly soluble precipitate which crystallises from water in plates and melts at 183°.

0·1682 gave 0·3395 CO_2 and 0·1377 H_2O. C = 55·04 ; H = 9·09.
0·1606 „ 9·4 c.c. nitrogen at 17° and 748 mm. N = 6·72.
$C_{10}H_{19}NO_4$ requires C = 55·29 ; H = 8·75 ; N = 6·45 per cent.

The amide is readily soluble in alcohol, sparingly so in cold water, ether, or benzene, and almost insoluble in light petroleum. When heated in a test tube, it gives off water and an oil distils which only partially solidified.

Methylisoamylhydroxysuccinamide is readily decomposed by boiling with potash solution and ammonia is evolved, but even when the potash is only in slight excess, some secondary decomposition takes place, and the resulting acid is difficult to obtain in a crystalline form. If, however, the amide is boiled with strong sodium carbonate solution, ammonia is only very slowly evolved, and even after 24 hours much of the compound remains unchanged and is precipitated on acidifying the alkaline liquid. The filtrate made alkaline with ammonia gives, on boiling with calcium chloride, a white, crystalline precipitate of calcium methylisoamylhydroxysuccinate, which is collected by the aid of a vacuum pump and washed with hot water, this salt being less soluble in hot than in cold water.

In order to obtain the free acid, the calcium salt was dissolved in dilute hydrochloric acid and the solution extracted several times with pure ether ; the ethereal solution, after drying over calcium chloride and evaporating, yielded a thick oil which, on standing over sulphuric acid in a vacuum desiccator, completely solidified. For the analysis, this acid was further purified by recrystallisation from a mixture of benzene and light petroleum.

I. 0·1896 gave 0·3863 CO_2 and 0·1430 H_2O. C = 55·56 ; H = 8·38.
II. 0·1701 „ 0·3441 CO_2 „ 0·1269 H_2O. C = 55·17 ; H = 8·29.
$C_{10}H_{18}O_5$ requires C = 55·04 ; H = 8·26 per cent.

Methylisoamylhydroxysuccinic acid melts at 66° and is very readily soluble in water, forming a strongly acid solution. It also dissolves readily in alcohol, and moderately so in benzene, but is almost insoluble in light petroleum.

The *silver* salt, $C_{10}H_{16}Ag_2O_5$, is obtained as a white precipitate on adding silver nitrate to a neutral solution of the ammonium salt.

0·2076 gave 0·2141 CO_2 and 0·0708 H_2O. C = 28·12 ; H = 3·78.
0·2380 „ 0·1181 Ag. Ag = 49·64.
$C_{10}H_{16}Ag_2O_5$ requires C = 27·91 ; H = 3·72 ; Ag = 50·0 per cent.

A neutral solution of the ammonium salt of the acid shows the following behaviour with reagents. *Barium chloride* gives a white, amorphous precipitate which becomes crystalline on boiling, and is

very sparingly soluble, even in boiling water. *Calcium chloride* forms no precipitate in the cold, but, on boiling, a very sparingly soluble, crystalline calcium salt separates. *Copper sulphate* gives a pale blue, amorphous precipitate, and *lead acetate*, a white, amorphous precipitate.

Methylisoamylmaleic Anhydride, $\begin{matrix} CH_3\cdot C\cdot CO \\ \| \\ C_5H_{11}\cdot C\cdot CO \end{matrix}\!\!>\!O$.

It was stated on p. 913 that the principal product of the hydrolysis of ethylic isoamylhydroxycyanobutyrate with alcoholic hydrochloric or sulphuric acid was an oil boiling constantly at 163° under 20 mm. pressure, which, on analysis, gave numbers agreeing approximately with those required by the formula $C_8H_{14}(COOC_2H_5)_2$.

This oil was hydrolysed by boiling with alcoholic potash for 2 hours, when, on adding water, a small quantity of oil separated, which, on examination, was found to consist of isoamylacetone. This oil was removed by extraction with ether, the alkaline solution was then acidified and repeatedly extracted with pure ether when, after drying over calcium chloride and evaporating, a thick, yellow oil was obtained which, even after long standing over sulphuric acid in a vacuum desiccator, showed no signs of crystallising. Ultimately, it was found that this product contained a small quantity of an acid which formed a sparingly soluble barium salt, and therefore the whole quantity was dissolved in a slight excess of ammonia and boiled with barium chloride. The insoluble barium salt was collected, washed with water, and dissolved in dilute hydrochloric acid, when, on extracting with ether, an acid was obtained which, on standing, solidified. The solid mass was spread on porous porcelain to remove traces of oily mother liquor, and recrystallised from a mixture of benzene and light petroleum. In this way glistening needles were obtained which melted at 66° and evidently consisted of methylisoamylhydroxysuccinic acid, as the following analysis and a careful comparison with a specimen of this acid, prepared as explained on p. 915, conclusively showed:

0·1346 gave 0·2708 CO_2 and 0·1 H_2O. C = 54·87; H = 8·25.
$C_{10}H_{18}O_5$ requires C = 55·04; H = 8·26 per cent.

The filtrate from the sparingly soluble barium salt was acidified, extracted with ether, and, after drying over calcium chloride and distilling off the ether, the residual oil fractionated under reduced pressure. After several distillations, an oil was obtained which boiled constantly at 142° under 16 mm. pressure, and which, on careful investigation, was found to consist of methylisoamylmaleic anhydride.

0·1856 gave 0·4460 CO_2 and 0·1348 H_2O. C = 65·54; H = 8·07.
$C_{10}H_{14}O_3$ requires C = 65·93; H = 7·69 per cent.

This anhydride is insoluble in cold sodium carbonate solution, but on warming with caustic soda it rapidly dissolves, and on acidifying and extracting with ether, an oil is obtained which is not the free acid, but the anhydride, since it is insoluble in sodium carbonate and, after standing for some time over sulphuric acid in a vacuum desiccator, it yielded the following results on analysis:

0·1860 gave 0·4436 CO_2 and 0·1333 H_2O. C = 65·04; H = 7·96.
Methylisoamylmaleic anhydride requires C = 65·93; H = 7·69 per cent.
,, acid requires C = 60·0; H = 8·0 per cent.

In order to obtain further evidence as to the mode of formation of methylisoamylmaleic anhydride, experiments were made with the object of determining whether this substance is formed when methylisoamylhydroxysuccinic acid is distilled at the ordinary pressure. On cautiously heating about 5 grams of the pure hydroxy-acid in a small fractionating flask, water was first given off and then the temperature rapidly rose to 255°, nearly the whole distilling between this temperature and 265°; on refractionating, an oil was obtained boiling constantly at 260—262°, which was insoluble in sodium carbonate solution.

That this oil was methylisoamylmaleic anhydride was shown by converting it into the anil which melted at 70°, and was identical in properties with the anil of methylisoamylmaleic acid described below. An equation representing the formation of the anhydride from methylisoamylhydroxysuccinic acid is given in the introduction.

Anil of Methylisoamylmaleic Acid, $\begin{matrix} CH_3\cdot C\cdot CO \\ C_5H_{11}\cdot C\cdot CO \end{matrix}\!\!>\!NC_6H_5$.

When a solution of methylisoamylmaleic anhydride in benzene is mixed with aniline, there is very little rise of temperature and no anilic acid separates on standing; if, however, the benzene is removed by evaporation on the water-bath and the residue then stirred with dilute hydrochloric acid, it gradually solidifies. The crystalline mass is spread on porous porcelain until quite free from oily mother-liquor, and then purified by crystallisation from dilute alcohol, from which it separates in glistening plates which melt at 70°.

0·1556 gave 0·4246 CO_2 and 0·1046 H_2O. C = 74·42; H = 7·47.
0·2412 ,, 12·3 c.c. nitrogen at 20° and 757 mm. N = 5·87.
$C_{16}H_{19}NO_2$ requires C = 74·71; H = 7·39; N = 5·44 per cent.

This anil is readily soluble in ether, benzene, warm alcohol, or light petroleum (b. p. 80—90°), sparingly so in water, and insoluble in sodium carbonate solution. When heated in small quantities, it distils apparently without decomposition.

Reduction of Methylisoamylmaleic Anhydride. Formation of cis- *and* trans-*Methylisoamylsuccinic Acids,* $\begin{matrix}CH_3\cdot CH\cdot COOH\\ C_5H_{11}\cdot CH\cdot COOH\end{matrix}$.

When methylisoamylmaleic anhydride (4 grams) is heated in a reflux apparatus on the sand-bath with fuming hydriodic acid (20 grams) and amorphous phosphorus (2 grams), reduction readily takes place, and after boiling for 8 hours and allowing to cool, a quantity of a crystalline substance separates. The product is diluted with twice its bulk of water, repeatedly extracted with ether, and the ethereal solution, after washing with dilute sodium bisulphite to remove iodine, dried over calcium chloride and evaporated, when a solid residue is obtained which consists of a mixture of the *cis*- and *trans*-acids. When this is stirred with light petroleum (b. p. 70—90°), the *cis*-acid dissolves, and leaves the almost pure *trans*-acid which, after recrystallising from water, is obtained in colourless prisms melting at 142°.

0·1686 gave 0·3676 CO_2 and 0·1337 H_2O. C = 59·46 ; H = 8·81.
$C_{10}H_{18}O_4$ requires C = 59·40 ; H = 8·91 per cent.

The light petroleum mother liquors of this acid, on evaporation, give a solid residue which crystallises from hydrochloric acid in plates melting at 92°, and consists of the *cis*-modification.

0·1534 gave 0·3328 CO_2 and 0·124 H_2O. C = 59·16 ; H = 8·98.
$C_{10}H_{18}O_4$ requires C = 59·40 ; H = 8·91 per cent.

These acids agree in all their properties with the *cis*- and *trans*-modifications of methylisoamylsuccinic acid which W. Trevor Lawrence has obtained by another process (Proc., 1899, **15**, 163).

Reduction of Ethylic Isoamylacetoacetate. Formation of α-Isoamyl-β-hydroxybutyric Acid, $CH_3\cdot CH(OH)\cdot CH(C_5H_{11})\cdot COOH$.

In investigating this reduction, ethylic isoamylacetoacetate (50 grams) was dissolved in alcohol (250 c.c.) and water (100 c.c.), and then treated in flat dishes with 3 per cent. sodium amalgam (2 kilos.) at ordinary temperatures, small quantities of water being added from time to time to facilitate the decomposition of the amalgam. After standing for 2 days and pouring into water, very little oil separated, showing that hydrolysis, as well as reduction, had taken place, and, in order to isolate the hydroxy-acid, the product was evaporated on the water-bath until free from alcohol, acidified, and extracted several times with pure ether. The ethereal solution was dried over calcium chloride and evaporated, when a thick oil was obtained, which, even on long standing, showed no signs of crystallising, but which can be

readily purified by conversion into the characteristic crystalline copper salt. In order to prepare this, the acid is dissolved in a slight excess of ammonia, and the moderately* dilute solution mixed with excess of copper sulphate and allowed to stand, when a beautifully crystalline, dark blue copper salt separates, which is collected, decomposed by hydrochloric acid, and the acid again extracted with ether. The oily acid thus obtained, after standing for some days over sulphuric acid in a vacuum desiccator, gave the following numbers on analysis:

0·1820 gave 0·4125 CO_2 and 0·1655 H_2O. C = 61·81; H = 10·10.
$CH_3 \cdot CH(OH) \cdot CH(C_5H_{11}) \cdot COOH$ requires C = 62·07; H = 10·34 per cent.

Isoamylhydroxybutyric acid is a thick, colourless oil, sparingly soluble in water, which, as shown below, distils under reduced pressure unchanged, but at the ordinary pressure decomposes on distillation into isoamylcrotonic acid and water.

The *silver* salt, $C_9H_{17}AgO_3$, was prepared by adding silver nitrate to a neutral solution of the ammonium salt. It is a white, amorphous precipitate, which, on analysis, gave the following result:

0·1233 gave 0·0477 Ag. Ag = 38·68.
$C_9H_{17}AgO_3$ requires Ag = 38·43 per cent.

A neutral and moderately strong solution of the ammonium salt gives a white, gelatinous precipitate with *barium chloride*, but no precipitate with *calcium chloride*.

α-Isoamylcrotonic Acid, $CH_3 \cdot CH{:}C(C_5H_{11}) \cdot COOH$.

When isoamylhydroxybutyric acid is distilled under reduced pressure (50 mm.), it passes over at about 195° without decomposition, as the following analysis of the distillate shows:

0·1755 gave 0·4 CO_2 and 0·1587 H_2O. C = 62·16; H = 10·04.
$CH_3 \cdot CH(OH) \cdot CH(C_5H_{11}) \cdot COOH$ requires C = 62·07; H = 10·34 per cent.

If, however, the distillation is conducted under the ordinary pressure, water is eliminated, and an oil passes over at 235—250°; this consists of crude isoamylcrotonic acid, and by repeatedly refractionating an oil is obtained boiling fairly constantly at about 240°. The analysis gave rather low results, due to some slight impurity, which could not be removed by fractionation.

0·1832 gave 0·4577 CO_2 and 0·1593 H_2O. C = 68·13; H = 9·66.
0·1336 ,, 0·3337 CO_2 ,, 0·1182 H_2O. C = 68·12; H = 9·83.
$CH_3 \cdot CH{:}C(C_5H_{11}) \cdot COOH$ requires C = 69·23; H = 10·25 per cent.

* It is important that the solution should not be too concentrated, otherwise the copper salt is apt to separate in resinous clumps.

Isoamylcrotonic acid is sparingly soluble in water, but dissolves readily in sodium carbonate, and the solution decolorises permanganate at once at the ordinary temperature.

The *silver* salt, obtained in the usual way, is a white, sparingly soluble, amorphous precipitate.

0·1956 gave 0·0815 Ag. Ag = 41·66.

$C_9H_{15}AgO_2$ requires Ag = 41·06 per cent.

Oxidation of Isoamylcrotonic Acid. Formation of Isobutylacetic Acid.—In investigating this oxidation, about 20 grams of the acid, in quantities of 5 grams at a time, were dissolved in a slight excess of very dilute sodium carbonate, and treated with potassium permanganate at 0° until the pink colour remained permanent for some hours; the excess of permanganate was then destroyed by sodium sulphite, and the filtrate from the manganese precipitate evaporated to a small bulk. On acidifying, an oily acid was precipitated, which was extracted with ether; the ethereal solution was very carefully dried over calcium chloride, evaporated, and the residual oil several times fractionated. In this way an acid was obtained boiling constantly at 202°, and showing all the properties of isobutylacetic acid, which, according to Lieben and Rossi (*Annalen*, 1871, **159**, 76), boils at 199·7° under 732 mm. pressure. The silver salt of this acid, prepared in the usual way, gave the following results on analysis:

0·2129 gave 0·2510 CO_2 and 0·0936 H_2O. C = 32·15; H = 4·88.

0·2021 „ 0·0974 Ag. Ag = 48·19.

$C_6H_{11}AgO_2$ requires C = 32·28; H = 4·93; Ag = 48·43 per cent.

β-Isoamyl-α-hydroxyisobutyric Acid, $\begin{matrix} C_5H_{11}\cdot CH_2 \\ CH_3 \end{matrix}\!\!>\!C(OH)\cdot COOH$.

This acid, which is isomeric with the α-isoamyl-β-hydroxybutyric acid described on p. 919, was obtained in small quantities in the following way:

Isoamylacetone (40 grams) was dissolved in dry ether (40 grams), finely-powdered potassium cyanide (30 grams) added, and then the calculated quantity of hydrochloric acid run in drop by drop, the whole being kept at −10° during the operation. After standing for 24 hours, the ethereal solution was washed and evaporated, and the residual oil hydrolysed by means of alcoholic hydrochloric acid, the method employed being exactly the same as that described on p. 912. On fractionating the product under reduced pressure (20 mm.), much unchanged isoamylacetone first passed over, then the temperature rose rapidly to 150°, most of the oil passing over between this and 170°, and on refractionating this, an oil was obtained boiling almost

constantly at 156° under 20 mm. pressure. Analysis showed that the composition of this oil varies, two different preparations giving respectively C = 79·27, H = 12·41, and C = 76·27, H = 11·97, whereas if the oil had consisted entirely of ethylic isoamylhydroxyisobutyrate, $C_5H_{11}\cdot CH_2\cdot C(OH)(CH_3)\cdot COOC_2H_5$, as was expected, the percentages would have been C = 65·34, H = 10·89.

The substance therefore contains some compound very rich in carbon and hydrogen, possibly produced by the condensation of two mols. of isoamylacetone under the influence of the reagents employed. On hydrolysing the oil with alcoholic potash, a large quantity of isoamylacetone was produced; this was removed by extracting with ether, the alkaline solution was then evaporated until free from alcohol, acidified, and repeatedly extracted with ether. After drying over calcium chloride and distilling off the ether, a small quantity of an oily acid was obtained, which soon solidified, and crystallised from light petroleum in glistening plates melting at 76°.

0·1318 gave 0·3 CO_2 and 0·1253 H_2O. C = 62·07; H = 10·56.
$C_9H_{18}O_3$ requires C = 62·07; H = 10·34 per cent.

The *silver* salt, $C_9H_{17}AgO_3$, was prepared from the neutral solution of the ammonium salt by adding silver nitrate. It is a white, amorphous precipitate, which, on analysis, gave the following result:

0·0937 gave 0·0364 Ag. Ag = 38·84.
$C_9H_{17}AgO_3$ requires Ag = 38·43 per cent.

There can be no doubt that this interesting acid is *β-isoamyl-α-hydroxyisobutyric acid*, but as the yield obtained by the method described above is only 1 per cent. of the isoamylacetone employed, it could not be investigated in more detail.

OWENS COLLEGE,
MANCHESTER.

RICHARD CLAY AND SONS, LIMITED, LONDON AND BUNGAY

THE ACTION OF ALUMINIUM CHLORIDE ON CAMPHORIC ANHYDRIDE.

BY

F. H. LEES

AND

W. H. PERKIN, JUN.

From the Transactions of the Chemical Society, 1901. Vol. 79.

XXXV.—*The Action of Aluminium Chloride on Camphoric Anhydride.*

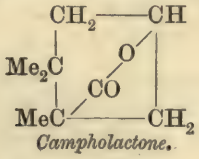
By F. H. Lees and W. H. Perkin, jun.

The behaviour of camphoric anhydride on treatment with aluminium chloride has already been made the subject of investigation, first by E. Burcker and subsequently by G. Blanc. E. Burcker (*Compt. rend.*, 1894, **119**, 426; *Bull. Soc. Chim.*, 1895, [iii], **13**, 901) studied the action of aluminium chloride on camphoric anhydride in the presence of benzene, and obtained in this way a crystalline substance, $C_{16}H_{20}O_3$, melting at 125—126°, and called by him *phenylcamphoric acid*, the corresponding yellowish liquid *anhydride*, $C_{16}H_{18}O_2$, a *ketonic acid*, $C_{15}H_{20}O_2$, which melted at 135—137°, and a *diphenyl* compound, $C_{22}H_{24}O_2$, which crystallised in reddish needles.

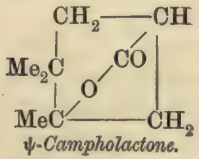
G. Blanc (*Compt. rend.*, 1896, **123**, 749; **124**, 468; *Bull. Soc. Chim.*, 1896, [iii], **15**, 1191; 1900, **23**, 693) then investigated the subject and showed that, when a solution of camphoric anhydride in chloroform is treated with aluminium chloride, an acid, $C_9H_{14}O_2$, of melting point 133°, which he subsequently identified as *isolauronolic acid*, is produced according to the equation $C_{10}H_{14}O_3 = C_9H_{14}O_2 + CO$, and this reaction now affords the most convenient method for preparing *iso*-lauronolic acid.

While we were engaged in the preparation of *iso*lauronolic acid by this process, we noticed that, besides this acid, an oil was always formed at the same time, and on investigating this, we found that it was apparently an almost pure substance, since, after twice fractionating, almost the whole quantity distilled constantly at 258° under ordinary conditions.

The analysis of this oil showed that it had the formula $C_9H_{14}O_2$, and on examination it was found to be a lactone so similar in properties to campholactone that we named it *ψ-campholactone* (Proc., 1899, **15**, 23), and suggested that the relationship between these two lactones was probably that represented by the formulæ

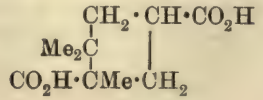


Campholactone.



ψ-Campholactone.

these formulæ being derived from



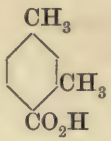
,

which at that time was considered to be the most probable expression of the constitution of camphoric acid.

As the result of a very extended investigation, we have found that this oily lactone, in spite of its remarkably constant boiling point, is a mixture of at least two isomeric lactones, $C_9H_{14}O_2$, and it appears that neither of these is directly related to campholactone. It will be seen, from the following description of our work, that we have changed our views as to the nature of this very interesting product of the action of aluminium chloride on camphoric anhydride.*

When the oily lactone is treated with baryta, it is readily hydrolysed, and the acid which is obtained by acidifying the resulting barium salt has been found to contain two hydroxy-acids of the formulæ $C_9H_{16}O_3$, which melt at 113° and 160° respectively.

Now when the original mixture of lactones or of their hydroxy-acids is dissolved in sulphuric acid and warmed at 80°, a remarkable decomposition takes place, much sulphur dioxide is evolved, and the solution on pouring into water deposits a solid acid which in each case has been proved to be *xylic acid*,



The easy transformation of these substances into xylic acid, as well as other properties which have been discovered during their investigation, leaves scarcely any doubt that they are all derivatives of hexahydro-xylic acid, and not in any direct way connected with camphoric acid; in other words, we are of opinion that the two acids, $C_9H_{16}O_3$, are stereoisomeric forms of *hydroxyhexahydro-xylic acid*,

$$OH \cdot C_6H_8(CH_3)_2 \cdot CO_2H.$$

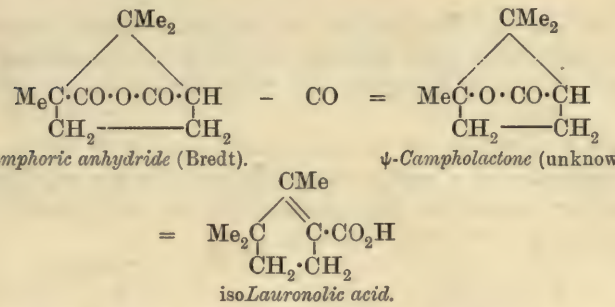
In endeavouring to obtain further evidence as to the probable constitution of these substances, it may be noted, in the first place, that *iso*lauronolic acid and the oily lactone mixture, $C_9H_{14}O_2$, are formed from camphoric anhydride by the removal of carbon monoxide:

$$2C_{10}H_{14}O_3 = \underset{\text{iso}\textit{Lauronolic acid.}}{C_9H_{14}O_2} + \underset{\textit{Oily lactones.}}{C_9H_{14}O_2} + 2CO.$$

If, then, we assume that the formula suggested by Bredt for camphoric acid is correct,† there can be scarcely any doubt that the conversion of camphoric anhydride into *iso*lauronolic acid must be represented thus:

* In the preliminary account of this work in the Proceedings (*loc. cit.*) we suggested that the lactone might, on further investigation, prove to be the lactone of hydroxyhexahydro-xylic acid.

† The reasons for adopting this formula will be discussed in a future paper.



Camphoric anhydride (Bredt). *ψ-Campholactone* (unknown). iso*Lauronolic acid.*

The isomeric change of *ψ*-campholactone into *iso*lauronolic acid necessitates the assumption of the migration of a methyl group from one carbon atom to the adjacent one; a change which is not unknown, as Dr. Lapworth pointed out in his paper, "On the Constitution of Camphor," at the Bradford meeting of the British Association.

Thus the transformation of *pinacone* into *pinacolin*,

$$\begin{matrix}\mathrm{CMe_2OH}\\ \mathrm{OH{\cdot}CMe_2}\end{matrix} = \begin{matrix}\mathrm{CMe_3}\\ \mathrm{O{:}CMe}\end{matrix} + \mathrm{H_2O},$$

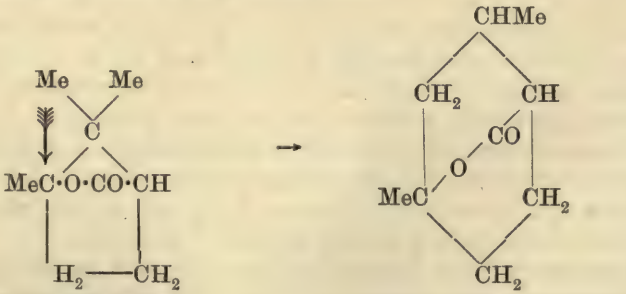
and of *pinacolyl alcohol* into *tetramethylethylene*,

$$\begin{matrix}\mathrm{CMe_3}\\ \mathrm{CHMe{\cdot}OH}\end{matrix} = \begin{matrix}\mathrm{CMe_2}\\ \mathrm{CMe_2}\end{matrix} + \mathrm{H_2O},$$

affords examples of an exactly similar migration of a methyl group. Very probably, isomeric changes of this nature will be found to take place frequently in the camphor group.

The formation of the lactones of hydroxyhexahydro-xylic acid during the action of aluminium chloride on camphoric anhydride is evidently a process of a different nature.

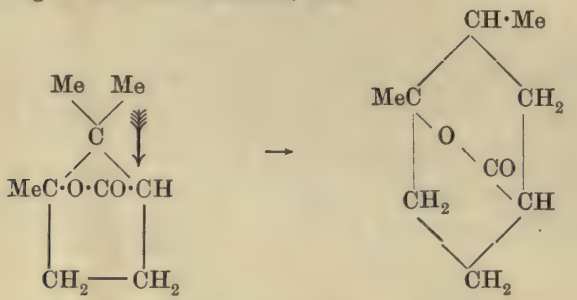
Apparently, the first stage is the same as that represented above in the case of *iso*lauronolic acid: the subsequent intramolecular change of the intermediate substance—*ψ*-campholactone—into a derivative of xylic acid may then be represented thus:



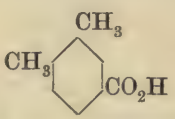
ψ-Campholactone. *Lactone of hydroxyhexahydro-xylic acid.*

In this case, one methyl of the $>CMe_2$ group enters the ring, and thus converts the original 5-membered ring into a 6-membered ring, a kind of isomeric change which has frequently been met with in the camphor series.

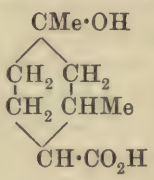
It may be noted at this stage that the formation of the lactones by the introduction of a methyl group into the ring can only take place in the way represented above, because if the methyl group were to enter the ring in the other direction, thus :



a lactone would be formed which is not a derivative of xylic acid, but of p-*xylic acid.*



If, then, the hydroxy-acids melting at 113° and 160° are hydroxy-hexahydro-xylic acids of the constitution

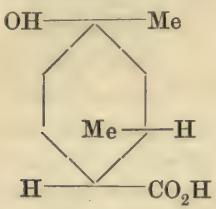


it would naturally be expected that, being δ-hydroxy-acids, they would *readily* form lactones, but this was not found to be the case, since aqueous solutions of these acids may be boiled for a considerable time without, apparently, a trace of lactone being formed.

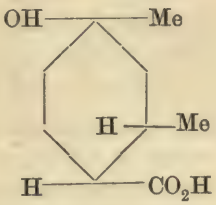
When, however, the acids are distilled, elimination of water takes place quantitatively, and two lactones are obtained ; that from the acid melting at 113° being crystalline and melting at 44°, whereas the lactone from the acid of melting point 160° is an oil.

Furthermore, these lactones on hydrolysis with baryta are reconverted into the acids from which they were obtained, showing that they are actually the lactones of these acids, and that no stereoisomeric

change has taken place at the high temperature of the distillation. Owing to the difficulty of lactone formation, we are inclined to believe that the two hydroxy-acids are the *trans*-modifications of hydroxy-hexahydro-xylic acid,



and



but until the corresponding *cis*-modifications have been isolated this view must remain doubtful, and in the meantime we propose to name the hydroxy-acid melting at 160° *A-hydroxyhexahydro-xylic acid*, and that melting at 113° *B-hydroxyhexahydro-xylic acid*.

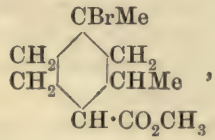
When the mixed lactones obtained by the action of aluminium chloride on camphoric anhydride are treated with phosphorus pentabromide and the product poured into methyl alcohol, a heavy oil is formed, which on fractionating yields a bromomethyl ester, $C_8H_{14}Br\cdot CO_2Me$, boiling at 165° under 30 mm., and a methyl ester, $C_8H_{13}\cdot CO_2Me$, boiling at 210° under 733 mm. pressure, the latter being formed by the elimination of hydrogen bromide from the former :

$$C_8H_{14}\begin{cases}CO\\O\end{cases} + PBr_5 = C_8H_{14}\begin{cases}COBr\\Br\end{cases} + POBr_3,$$

$$C_8H_{14}\begin{cases}COBr\\Br\end{cases} + CH_3\cdot OH = C_8H_{14}\begin{cases}CO_2CH_3\\Br\end{cases} + HBr$$

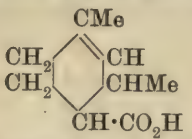
$$C_8H_{14}Br\cdot CO_2CH_3 = C_8H_{13}\cdot CO_2CH_3 + HBr.$$

The former of these is *methyl bromohexahydro-xylate*,

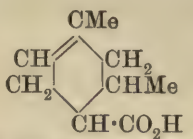


and the latter substance, which may be obtained almost quantitatively by digesting the bromomethyl ester with diethylaniline, is *methyl tetrahydro-xylate*. On hydrolysis, methyl tetrahydro-xylate yields the corresponding *tetrahydro-xylic acid*, a colourless, crystalline substance which melts at about 72°, and shows all the properties of an unsaturated acid. So far, it has not been found possible to definitely assign a constitutional formula to this new acid, since the elimination of

hydrogen bromide from bromohexahydro-xylic acid may take place in two directions, giving the following acids:



Δ^4-*Tetrahydro-xylic acid.*



Δ^3-*Tetrahydro-xylic acid.*

Besides this tetrahydro-xylic acid of melting point 72°, which we have reason to believe corresponds to the hydroxy-acid melting at 160°, there is also formed, when the methyl tetrahydro-xylate mentioned above is hydrolysed, a second tetrahydro-xylic acid, which perhaps corresponds to the hydroxy-acid melting at 113°.

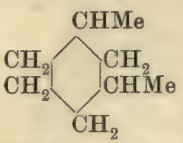
This acid has, so far, only been obtained as an oil, probably because it could not be entirely freed from the tetrahydro-xylic acid of melting point 72°; when obtained in a pure state, it will very likely be found to be crystalline.

One of the most remarkable properties of tetrahydro-xylic acid (m. p. 72°) is the ease with which it is converted into xylic acid on treatment with sulphuric acid; as this change not only takes place very readily at 70—80°, but even at the ordinary temperature, sulphur dioxide is slowly evolved, and after standing for 4 weeks, it is found that a quantity of xylic acid has been produced, a transformation which seems to us to be very strong evidence in support of our contention that this acid is a tetrahydro-xylic acid.

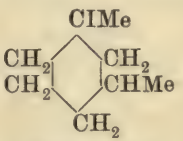
In order, however, to obtain still more positive confirmation of our view that the substances described in this paper are derivatives of xylic acid, a number of experiments were instituted on the reduction of the mixed lactones with hydriodic acid, with results which, although not so decisive as could have been wished, nevertheless point in the same direction. When the mixed lactones are heated with fuming hydriodic acid at 180°, reduction readily takes place, and the product is found to consist of a *hydrocarbon*, C_8H_{16}, of boiling point 119°; an *iodide*, $C_8H_{15}I$, boiling at 115° under 32 mm. pressure, and an *acid*, $C_8H_{15}\cdot CO_2H$, which boils at 248—253°.

The hydrocarbon is evidently *hexahydro*-m-*xylene* and identical with the substance of this constitution which has already been obtained by heating camphoric acid at 280° with hydriodic acid and in other ways (see p. 349), the iodide is probably *iodohexahydro*-m-*xylene* [1 : 1 : 3] and isomeric with the *iodohexahydro*-m-*xylene* [1 : 3 : 5] of Knoevenagel (see p. 349) and the acid is doubtless a mixture of the stereoisomerides of *hexahydro-xylic acid*, but the small yield produced during this reduction has not, so far, allowed of our separating these isomerides.

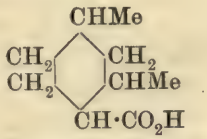
The constitution of these products of the action of hydriodic acid on the mixed lactones is readily understood from the following formulæ:



Hexahydro-m-*xylene.*



Iodohexahydro-m-*xylene* (1 : 1 : 3).



Hexahydro-xylic acid.

and their formation is undoubtedly confirmatory evidence of our view that the compounds described in this paper are derivatives of xylic acid. As so much of the material used in these experiments with hydriodic acid was converted into neutral substances, we next tried to reduce a large quantity of the mixed tetrahydro-xylic acids as they are obtained by the hydrolysis of the methyl tetrahydro-xylate mentioned on page 352, but although we used sodium and boiling amyl alcohol as the reducing agent, and carried out the operation four times with the same material, only about 5 per cent. of the unsaturated acid was reduced, yielding an oily acid, $C_8H_{15}\cdot CO_2H$, which again doubtless consisted of a mixture of the stereoisomeric modifications of hexahydro-xylic acid.

In the preparation of *iso*lauronolic acid and the mixed lactones of hydroxyhexahydro-xylic acid by the action of aluminium chloride on camphoric anhydride, the process is complete in a few hours, and the product was usually worked up after standing for 15 hours. On one occasion, however, the mixture was allowed to remain in a cool place for four weeks, when, on treating the product in the usual way, about the same quantity of the mixed lactones was obtained, although, curiously enough, the *iso*lauronolic acid, which must have been present at first, had almost entirely disappeared.

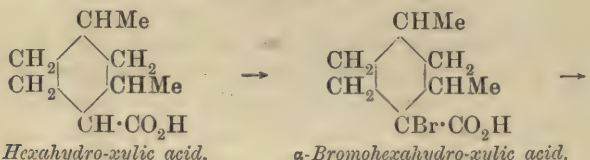
In the place of this acid, a quantity of a liquid acid was obtained which boiled constantly at 155° under 30 mm. pressure and consisted principally of a saturated acid, $C_8H_{15}\cdot CO_2H$, mixed with varying quantities of an unsaturated acid, which was apparently tetrahydro-xylic acid.

After removing the unsaturated acid by oxidation and exposing the distilled saturated acid to a low temperature, crystals melting at 75° separated, and these on examination were found to consist of the modification of hexahydro-xylic acid which Bentley and Perkin obtained by the direct reduction of xylic acid (Trans., 1897, 71, 173). The proof of this was obtained in the following way.

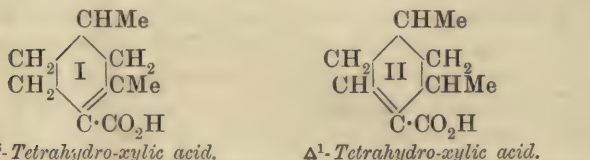
The crystals were treated with bromine and phosphorus trichloride and the product poured into methyl alcohol, when *meth*

α-bromohexahydro-xylate was obtained as a colourless oil boiling at 143—146° under 35 mm. pressure. This, when hydrolysed with excess of alcoholic potash, yields an acid melting at 106°, which is identical with the tetrahydro-xylic acid obtained by Bentley and Perkin (*loc. cit.*)* by the reduction of xylic acid with sodium and amyl alcohol, as a direct comparison of the two specimens clearly showed.

From its method of formation, this tetrahydro-xylic acid may have two formulæ, as will be seen from the following:



Hexahydro-xylic acid. *α-Bromohexahydro-xylic acid.*



Δ^6-*Tetrahydro-xylic acid.* Δ^1-*Tetrahydro-xylic acid.*

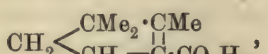
At this stage of our experiments, it is not possible to definitely decide between these two formulæ, but the behaviour of the acid with bromine, and especially on oxidation with permanganate, has led us to the conclusion that it is Δ^6-tetrahydro-xylic acid and has the constitution represented by formula I.

Since, then, it is proved that *iso*lauronolic acid, on long contact with aluminium chloride under the conditions described on p. 356, is converted into hexahydro-xylic acid—a process not only of molecular change but also of reduction,

$$\underset{\text{iso}\textit{Lauronoli acid.}}{C_8H_{13}\cdot CO_2H} + 2H = \underset{\textit{Hexahydro-xylic acid.}}{C_8H_{15}\cdot CO_2H}$$

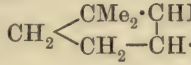
it is obviously interesting to endeavour to understand how this remarkable change takes place.

There is, at the present time, scarcely any doubt that the constitution of *iso*lauronolic acid is represented by the formula

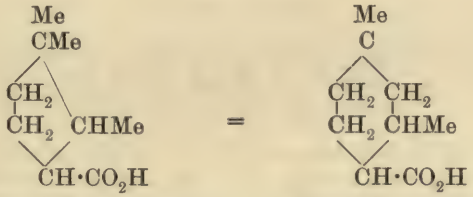


* The melting point, 103°, given by Bentley and Perkin for this acid is too low; it should be 106°.

and it is known that this acid on reduction is readily converted into dihydro*iso*lauronolic acid,



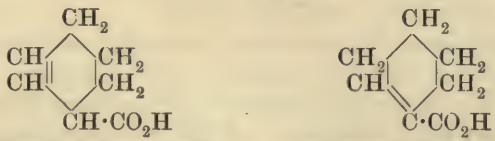
If now we compare this last formula with that of hexahydro-xylic acid, we see, at once, that in order to produce the latter from the former it is only necessary for one methyl of the $>CMe_2$ group to migrate into the ring, and thus convert the 5-membered ring of dihydro*iso*lauronolic acid into the 6-membered ring of hexahydro-xylic acid, a change similar to that referred to on p. 334 in discussing the formation of the lactone of hydroxyhexahydro-xylic acid :



*Dihydro*isolauronolic acid. *Hexahydro-xylic acid.*

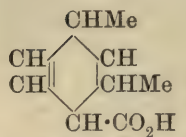
It has already been mentioned that tetrahydro-xylic acid (m.p. 107°) was first obtained by Bentley and Perkin (*loc. cit.*) by reducing xylic acid, dissolved in boiling amyl alcohol with sodium, and now that this acid has been obtained by the hydrolysis of methyl-*a*-bromohexahydro-xylate, and it has thus been proved that the double bond must be attached to the same carbon atom as the carboxyl group, interesting evidence is obtained as to the course which the reduction of xylic acid follows under the conditions mentioned above.

Aschan (*Ber.*, 1891, **24**, 1865 ; *Annalen*, 1892, **271**, 234) has shown that benzoic acid on reduction with sodium amalgam is first converted into Δ^2-tetrahydrobenzoic acid, and that this acid on boiling with strong alkalis undergoes isomeric change into Δ^1-tetrahydrobenzoic acid :

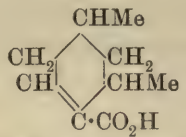


Δ^2-*Tetrahydrobenzoic acid.* Δ^1-*Tetrahydrobenzoic acid.*

In the case of xylic acid, the reduction would be expected to pursue a similar course, yielding in the first place Δ^2-tetrahydro-xylic acid, which then would be converted into the Δ^1-acid by boiling with alkali.



Δ^2-*Tetrahydro-xylic acid.*



Δ^1-*Tetrahydro-xylic acid.*

Since, however, in the experiments of Bentley and Perkin on the reduction of xylic acid, sodium and boiling amyl alcohol were employed, both reduction and the isomeric change from Δ^2 to Δ^1 would be expected to take place simultaneously, and it is therefore easy to understand that Δ^1-tetrahydro-xylic acid was the acid actually obtained.

Experimental.

The Action of Aluminium Chloride on Camphoric Anhydride. Preparation of iso*Lauronolic Acid and of the Mixed Lactones of Hydroxyhexahydro-xylic Acid.*

In studying this reaction, a very large number of experiments were made, principally with the view to determining the conditions which give the largest yield of the lactones, and as the result of these we ultimately adopted the following method.

Carefully dried camphoric anhydride (100 grams) is dissolved in pure dry chloroform (400 c.c.) in a flask fitted with a cork through which a long tube passes, in order that the gases produced during the subsequent reaction may be led away through the draught-hole of the draught-cupboard or into the open air. One hundred grams of the best aluminium chloride prepared from aluminium * is then added, when in a short time a vigorous reaction commences, accompanied by the evolution of carbon monoxide and hydrogen chloride, but as no great rise of temperature takes place, it was rarely necessary to cool the flask, this being only done when the temperature rose above about 45°. After about 15 minutes, the decomposition becomes much quieter, and it is curious that there always seems to be a slight absorption of heat towards the end of the reaction.

The whole mass is allowed to stand overnight, and then mixed with 1½ litres of water, when large quantities of aluminium hydroxide are precipitated; strong potash solution is now added until the precipitate has been completely dissolved, and the chloroform layer containing the lactones separated from the alkaline solution which contains the *iso*lauronolic acid. The aqueous solution is extracted once with chloroform, and the combined chloroform solutions washed three

* The quality of the aluminium chloride seems to have a very marked influence on the course of the reaction; we obtained our supply from Kahlbaum in sealed tubes of 100 grams.

times with water, dried over calcium chloride, and the chloroform distilled off, when a light brown oil is obtained which, on fractionation under reduced pressure (50 mm.), distils almost completely at 164—170°, and on refractionation almost the whole boils constantly at 164—166° under the same pressure. Two different preparations were analysed with the following results:

0·1940 gave 0·4960 CO_2 and 0·1578 H_2O. C = 69·7; H = 9·0.
0·1732 „ 0·4447 CO_2 „ 0·1419 H_2O. C = 70·0; H = 9·1.
$C_9H_{14}O_2$ requires C = 70·1; H = 9·1 per cent.

This oil, which is a mixture of the lactones of two of the modifications of *hydroxyhexahydro-xylic acid* (see p. 344), has a peculiar sweet smell, and distils under the ordinary pressure at 260° as a colourless oil which on standing becomes brown. It is insoluble in sodium carbonate and in caustic potash solution in the cold, but dissolves easily in the latter on warming, and the solution gives no precipitate on acidifying in the cold, but, on boiling, oily drops of a lactone soon separate. The lactone is volatile in steam, and somewhat soluble in water. The density, refraction, and magnetic rotation of the oil boiling at 164—166° (50 mm.) were determined before it was known that it was a mixture of stereoisomeric modifications, and we give these numbers because the stereoisomerism may have little effect on refraction and magnetic rotation, and the numbers may therefore still be valuable.

Density determinations: d 4°/4° = 1·0652; d 10°/10° = 1·0606; d 15°/15° = 1·0571; d 20°/20° = 1·0538; d 25°/25° = 1·0512.

Magnetic rotation.

t.	Sp. rotation.	Mol. rotation.
15·6°	1·0128	8·200

Refractive power.

d 18·5°/4° = 1·05327.

	μ 18·5°.	$\frac{\mu-1}{d}$	$\frac{\mu-1}{d}p$.
H_α	1·4692	0·44547	68·603
H_β	1·47760	0·45345	69·831
H_γ	1·48254	0·45814	70·553

The specimens examined had a slight permanent rotation equal to about − 2° for a length of 102 mm.

Several experiments on the oxidation of the oily lactone were made, but with very unsatisfactory results. When dissolved in dilute potash and treated at the ordinary temperature with daily additions

of small quantities of permanganate, oxidation takes place slowly, and after three weeks, when the action had become very sluggish, the product on examination was found to contain, besides large quantities of oxalic acid, an oily ketonic acid, which, however, was produced in such small quantity that we were unable to purify it.

Isolation and Purification of iso*Lauronolic Acid.*—As stated in a previous paper (Trans., 1898, 73, 801), the most convenient way of preparing *iso*lauronolic acid in quantity, is by treating camphoric anhydride with aluminium chloride, and several kilos. of this acid have been prepared by this method for experiments on the investigation of its constitution.

The best way to isolate the acid from the strongly alkaline extract which had been separated from the chloroform solution of the lactones, as explained on p. 341, is as follows.

After every trace of chloroform has been removed by a current of air, the clear solution is mixed with an excess of hydrochloric acid, when an ochre-coloured precipitate is thrown down, which, although somewhat sticky at first, should, on standing, become quite hard. This precipitate is dissolved in ammonia and submitted to distillation in steam, by which means the ammonium salt of *iso*lauronolic acid is dissociated, and the acid distils with the steam and ammonia.

The distillate deposits, on acidifying, a white, flocculent precipitate which melts at 127—132°, and consists of almost pure *iso*lauronolic acid, and two crystallisations from dilute acetic acid raises the melting point to 133—134°, the correct melting point of the acid.

This method of purification has been found much more convenient than that recommended by Blanc, which consists in separating the crude mixture of acids formed in the reaction by recrystallisation from alcohol. The yield of *iso*lauronolic acid obtained by the above process is from 40—50 per cent. of the camphoric anhydride employed.

After all the *iso*lauronolic acid has distilled over with the steam in the way described above, the distillation flask contains a thick oil, which, as the liquid cools, solidifies to a hard, brown button; this generally adheres firmly to the side of the flask, and on acidifying the aqueous solution of the undissociated ammonium salt, a quantity of an amorphous acid separates in white flocks. This acid is very difficult to obtain in a crystalline condition, but on one occasion the crude acid was dissolved in dilute sodium carbonate, the solution boiled with animal charcoal, and, after filtering, acidified with hydrochloric acid, when a white, amorphous precipitate was obtained, which crystallised from acetic acid in glistening needles, and melted at 255—257°. On analysis:

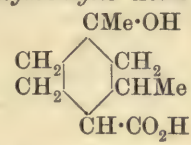
0·1584 gave 0·3911 CO_2 and 0·1196 H_2O. C = 67·3; H = 8·4.
$C_{11}H_{16}O_3$ requires C = 67·3; H = 8·2 per cent.

The *silver* salt was obtained by adding silver nitrate to a neutral solution of the ammonium salt as a white, amorphous precipitate which was very difficult to wash. On analysis:

0·2407 gave 0·3670 CO_2, 0·1090 H_2O, and 0·0885 Ag. C = 41·6; H = 5·0; Ag = 36·7.
$C_{11}H_{15}O_3Ag$ requires C = 43·5; H = 4·9; Ag = 35·7 per cent.

We were not able to repeat the preparation and analysis of this silver salt, and cannot, therefore, be sure that this well characterised acid really has the constitution $C_{11}H_{16}O_3$. The acid, which may be formed by the chloroform reacting with the camphoric anhydride in the presence of the aluminium chloride, contains no chlorine; it is readily oxidised by nitric acid, and its solution in sodium carbonate at once decolorises permanganate.

The Hydroxyhexahydro-xylic Acids and their Lactones,



When the mixed lactones obtained by the action of aluminium chloride on camphoric anhydride are heated on the water-bath with excess of baryta water, the oily drops rapidly dissolve with formation of the barium salts of the corresponding hydroxy-acids. If the excess of baryta is removed by passing carbon dioxide through the boiling liquid, and, after filtering, the filtrate is evaporated on the water-bath, a thick, syrupy barium salt is obtained which even on long standing shows no signs of crystallising. The syrupy salt was dissolved in a little water, acidified with a slight excess of hydrochloric acid, and the hydroxy-acids, which separated as a thick, pale yellow oil, extracted with pure ether. After drying over calcium chloride, the bulk of the ether was distilled off, the remainder being removed by aspirating dry air through the solution, and in this way all rise of temperature above 40° was avoided. The resulting thick syrup, after standing for some weeks in a cold place, deposited a considerable quantity of crystals, which were collected on the pump and left in contact with porous porcelain until free from oil.* The colourless

* This oil still contains considerable quantities of the mixed hydroxy-acids, A and B, along with other substances, a description of which is reserved for a future paper.

crystals thus obtained consist of the A-hydroxy-acid (m. p. 160°) mixed with varying quantities of the B-hydroxy-acid (m. p. 113°), and these two acids may be separated by dissolving in pure dry ether, evaporating to a small bulk, and allowing to stand, when a crystalline crust of the A-acid rapidly separates often in an almost pure state, the B-acid, which is much more soluble, remaining in the mother liquor. By repeating the crystallisation, the A-acid is very easily obtained in a pure condition. On analysis:

0·1546 gave 0·3554 CO_2 and 0·1308 H_2O. C = 62·7; H = 9·4.
0·1393 „ 0·3204 CO_2 „ 0·1170 H_2O. C = 62·7; H = 9·3.
$C_9H_{16}O_3$ requires C = 62·8; H = 9·3 per cent.

A-hydroxyhexahydro-xylic acid melts at 160° without decomposition. It is moderately soluble in hot, but sparingly so in cold water, and is very sparingly soluble in pure, dry ether.

It crystallises very well from water in the form of feathery leaf-like plates.

It dissolves readily in sodium hydrogen carbonate and the solution does not decolorise permanganate, except on long standing.

The *silver* salt, $C_8H_{14}(OH)\cdot CO_2Ag$, obtained on adding silver nitrate to a neutral solution of the ammonium salt, was a white, gelatinous precipitate which, on warming, became granular and was easily washed. On analysis:

0·2031 gave 0·0777 gram Ag. Ag = 38·3.
$C_9H_{15}O_3Ag$ requires Ag = 38·6 per cent.

A neutral solution of the ammonium salt gives no precipitate with either barium or calcium chlorides; with copper sulphate, no precipitate is produced in the cold, but on warming, a sparingly soluble pale blue copper salt separates.

Lactone of A-Hydroxyhexahydro-xylic acid, $C_8H_{14}<\begin{matrix}O\\|\\CO\end{matrix}$.—In order to determine whether the A-hydroxy-acid readily yielded a lactone, 2 grams were dissolved in water and subjected to rapid distillation in steam for 1 hour. The distillate, on saturating with ammonium sulphate and repeatedly extracting with ether, did not yield even a trace of lactone, and on evaporating the residue in the distilling flask to a small bulk and allowing to stand for a few days, nearly the whole of the unchanged acid separated in colourless crystals, showing that under these conditions the A-hydroxy-acid does not yield a lactone. Further experiments showed, however, that this lactone is readily obtained by simply distilling the hydroxy-acid. About 5 grams of the pure dry acid were introduced into a small fractionating flask and gently heated until the elimination of water, which commences at

about 175°, was complete; the temperature was then raised, when practically the whole of the residue distilled at 260—263° as a colourless oil. This oil was dissolved in ether, the ethereal solution washed with sodium carbonate to remove a small quantity of an acid substance which was present, dried over calcium chloride, evaporated, and the residue rapidly distilled, when almost the whole quantity passed over at 261—262° under 748 mm. pressure. On analysis:

0·2143 gave 0·5456 CO_2 and 0·1806 H_2O. C = 69·4; H = 9·4.
0·1783 „ 0·4575 CO_2 „ 0·1480 H_2O. C = 69·9; H = 9·2.
$C_9H_{14}O_2$ requires C = 70·1; H = 9·1 per cent.

The *lactone* of *A-hydroxyhexahydro-xylic acid* is a colourless oil which, when cooled in a freezing mixture, showed no signs of crystallising. That it is really the lactone of the A-hydroxy-acid and that no isomeric change had taken place at the high temperature of the distillation is shown by the following experiment. About 2 grams of the lactone were warmed with baryta water until dissolved, the well-cooled solution was then acidified with hydrochloric acid, and extracted several times with pure ether. After carefully drying with calcium chloride and evaporating to a small bulk, the ethereal solution deposited a crust of colourless crystals which melted at 160°, and on examination were found to consist of the pure A-hydroxy-acid.

B-Hydroxyhexahydro-xylic Acid.—The ether mother liquors from the purification of the A-hydroxy-acid (p. 345) yield, on concentrating, several crops of crystals consisting of the B-acid mixed with varying quantities of the A-acid, and by a long series of fractional crystallisations it is ultimately possible to obtain the much more readily soluble B-acid in a state of purity. On analysis:

0·1355 gave 0·3110 CO_2 and 0·1132 H_2O. C = 62·6; H = 9·3.
0·1490 „ 0·3426 CO_2 „ 0·1254 H_2O. C = 62·7; H = 9·3.
$C_9H_{16}O_3$ requires C = 62·8; H = 9·3 per cent.

B-Hydroxyhexahydro-xylic acid melts at 113°, but the presence of traces of the A-acid frequently lowers the melting point to 109—110°. It is much more readily soluble in water than the A-acid, and its aqueous solution on slowly evaporating over sulphuric acid deposits the hydroxy-acid in hard prisms, closely resembling crystals of cane sugar, and quite different in appearance from the leafy crystals of the A-acid.

The moderately dilute solution of the ammonium salt gives no precipitate with silver nitrate at first, but, on standing, gelatinous flocks gradually separate in small quantities. These were filtered off, and the solution concentrated on the water-bath, when after filtering from a few brown flocks, the filtrate on cooling set to a colourless jelly,

and all attempts to wash this and thus obtain the silver salt in a pure condition were unavailing.

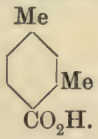
In other respects, the neutral solution of the ammonium salt shows a similar behaviour with reagents to that of the A-hydroxy-acid.

Lactone of B-Hydroxyhexahydro-xylic Acid.—As in the case of the A-hydroxy-acid, we first experimented with the view of determining whether the B-hydroxy-acid is converted into its lactone by boiling with water. The pure B-hydroxy-acid (2 grams) was dissolved in water and the solution distilled in steam for 1 hour, exactly as described in the case of the A-hydroxy-acid (p. 345). The distillate, on extraction with ether, did not yield any lactone, and from the residue in the distilling flask nearly the whole of the B-hydroxy-acid was recovered unchanged. It is therefore evident that this acid is not converted into its lactone on boiling with water. The lactone may, however, be obtained almost quantitatively by distilling the pure B-hydroxy-acid exactly as described in the case of the A-acid (p. 346). The distillate was dissolved in ether and extracted repeatedly with sodium carbonate. The ethereal solution was then dried and evaporated, and the residual oil carefully fractionated. After two distillations, almost the whole quantity passed over at 260° under 758 mm. pressure as a colourless oil which, on cooling and rubbing with a glass rod, solidified completely to a hard mass of crystals melting at 38—40°. This lactone is sparingly soluble in light petroleum, and if the solution is allowed to evaporate spontaneously, feathery groups are gradually formed which melt at 44°, and consist of the pure lactone of the B-hydroxy-acid. On analysis:

0·1850 gave 0·4755 CO_2 and 0·1528 H_2O. C = 70·1 ; H = 9·2.
$C_9H_{14}O_2$ requires C = 70·1 ; H = 9·1 per cent.

That this substance is the *lactone* of *B-hydroxyhexahydro-xylic acid*, is proved by the fact that when hydrolysed with baryta a hydroxy-acid is produced which, after extraction with ether and evaporation to a small bulk, is deposited in hard crystals which melt at 110—112°, and show all the properties of the B-hydroxy-acid.

Action of Sulphuric Acid on the Lactones of the Hydrohexahydro-xylic Acids. Formation of Xylic Acid,



It has already been mentioned in the introduction to this paper that the mixed lactones when heated with sulphuric acid are rapidly

oxidised with formation of xylic acid, and the actual experiment was carried out as follows.

The mixed lactones (5 grams) were dissolved in concentrated sulphuric acid (50 grams) and warmed in a water-bath the temperature of which was kept at between 80° and 85°. In a short time, the solution began to darken in colour, and there was much effervescence due to the escape of sulphur dioxide; when this had ceased, which was usually the case after about 10 minutes heating, the dark brown liquid was cooled and poured into three times its volume of water. After well stirring and allowing to stand overnight, the greyish coloured sandy precipitate was collected, dried, and rapidly distilled from a small retort. The crystalline distillate was dissolved in sodium carbonate, the solution boiled with animal charcoal, filtered, and the hot filtrate acidified, when an almost colourless, crystalline precipitate was thrown down which consisted of nearly pure xylic acid. After crystallising from dilute acetic acid, the substance was obtained as a colourless crystalline powder which melted at 126°. On analysis:

0·1600 gave 0·4220 CO_2 and 0·0984 H_2O. C = 71·9; H = 6·8.
0·1620 „ 0·4261 CO_2 „ 0·0976 H_2O. C = 71·7; H = 6·7.
$C_9H_{10}O_2$ requires C = 72·0; H = 6·7 per cent.

Some of this acid was intimately mixed with an equal quantity of pure xylic acid prepared from ψ-cumene, without any alteration in the melting point being produced, a proof that the two acids were identical. In order, however, to be certain of this, a quantity of the acid was converted into the *anilide*, which, after crystallising from light petroleum (b. p. 80—100°), melted at 140—141°. On analysis:

0·0763 gave 4·3 c.c. nitrogen at 18° and 757 mm. N = 6·4.
$C_{15}H_{15}ON$ requires N = 6·2 per cent.

A direct comparison of this anilide with a specimen of the anilide of xylic acid showed that the two specimens were identical.

Action of Hydriodic Acid on the Lactones of Hydroxyhexahydro-xylic Acid.

In order to determine whether it was possible to reduce these lactones directly to hexahydro-xylic acid, 25 grams of the mixed lactones were heated with 100 grams of fuming hydriodic acid (sp. gr. 1·96) and a little amorphous phosphorus in sealed tubes at 180° for 3 hours. There was much pressure in the tubes and on pouring the contents, which were highly coloured with iodine, into dilute sulphurous acid, a heavy oil separated and was extracted with ether. The ethereal solution was repeatedly washed with small quantities of dilute potash, dried over calcium chloride, and evaporated, when a colourless oil remained which smelt strongly of hexyl iodide.

This oil was distilled from a fractionating flask, at first under the ordinary pressure, when a quantity of oil came over below 150°; the residue, which was fractionated under reduced pressure (20 mm.) distilled at 110—120°, leaving a slight residue smelling of phosphorus compounds. The first portion on repeated fractionation distilled constantly at 119°, but contained traces of iodine; it was therefore digested with sodium and again distilled, when the whole passed over at 119°, under 760 mm. pressure, but still contained faint traces of iodine. On analysis:

0·1785 gave 0·5569 CO_2 and 0·2273 H_2O. C = 85·1; H = 14·2.

The substance was again distilled over sodium and was now free from iodine. On analysis:

0·1610 gave 0·5042 CO_2 and 0·2056 H_2O. C = 85·4; H = 14·2.
C_8H_{16} requires C = 85·71; H = 14·3 per cent.

This hydrocarbon is saturated, since it does not decolorise permanganate and is not attacked by bromine at the ordinary temperature.

A careful comparison of the properties of this hydrocarbon with those of known saturated hydrocarbons of the formula C_8H_{16} leads at once to the conclusion that it is *hexahydro*-m-*xylene*. This hydrocarbon has been obtained by heating camphoric acid at 280° with hydriodic acid (Wreden, *Annalen*, 1877, **187**, 155), and also from heptanaphthenecarboxylic acid by similar treatment (O. Aschan, *Ber.*, 1891, **24**, 2718), and is described as a mobile liquid boiling at 119° under 755 mm. pressure and stable towards bromine. The latter method of formation, taken in connection with the present experiments, is instructive, and indicates that it may be a common property of saturated closed chain carboxylic acids when heated with hydriodic acid to lose carbon dioxide and yield the corresponding hydrocarbon.

The oil separated from the hexahydro-*m*-xylene by fractionation under reduced pressures and boiling at 110—120° under 20° mm. pressure was twice carefully refractionated, when almost the whole distilled at 113—115° under 32 mm. pressure with elimination of a little hydrogen iodide. This oil, which rapidly became dark coloured owing to the separation of iodine, was analysed, with the following results:

0·1486 gave 0·2280 CO_2 and 0·0923 H_2O. C = 41·84; H = 6·9.
0·2067 „ 0·1983 AgI. I = 51·81.
$C_8H_{15}I$ requires C = 40·4; H = 6·3; I = 53·36 per cent.

It is very probable that this substance is iodohexahydro-*m*-xylene [1:1:3] and isomeric with the iodohexahydro-*m*-xylene [1:3:5] boiling at 92—93° under 10 mm. pressure, which Knoevenagel (*Annalen*, 1897,

297, 163) obtained by the action of hydriodic acid on dimethyl-1 : 3-*cyclo*hexanol-5.

The alkaline liquid obtained by extracting the ethereal solution of the crude product of the reduction of the lactone with potash in the way described above gave on acidifying with hydrochloric acid and extracting with ether in the usual way, 8 grams of a thick, oily acid. On fractionating this under reduced pressure (25 mm.) about half passed over between 160° and 175°, leaving a viscid residue which contained phosphorus and did not distil until above 300°. The fraction boiling at 160—175° under 25 mm. pressure was twice distilled under the ordinary pressure and in this way 2 grams of an oil were obtained which distilled at 248—253°. On analysis:

0·1460 gave 0·3680 CO_2 and 0·1329 H_2O. C = 68·74 ; H = 10·11.

$C_9H_{16}O_2$ requires C = 69·23 ; H = 10·25.

There can scarcely be a doubt that this acid is hexahydro-xylic acid, $C_8H_{15}\cdot CO_2H$, produced by the direct reduction of the lactone.

Action of Phosphorus Pentabromide on the Lactones of the Hydroxyhexahydro-xylic Acids.

When the lactone and phosphorus pentabromide are mixed in molecular proportion, the pentabromide rapidly dissolves with considerable rise of temperature and evolution of some hydrogen bromide. If the product after standing for some time is heated for a few minutes on the water-bath and then poured into methyl alcohol, two substances are produced, namely, *methyl bromohexahydro-xylate* and *methyl tetrahydro-xylate*.

In order to isolate the product of the reaction, the methyl alcohol solution is poured into much water, the heavy oil which separates extracted with ether, the ethereal solution washed with water and dilute sodium carbonate, dried over calcium chloride, and the ether distilled off. The residual oil is then fractionated under reduced pressure (40 mm.) and thus roughly separated into two portions boiling at 120—135° and 135—180° respectively. From the latter, by repeated fractionation, a pungent smelling oil may be obtained boiling at 160—165° under 30 mm. pressure and consisting of *methyl bromohexahydro-xylate*, $C_8H_{14}Br\cdot CO_2CH_3$. On analysis:

0·3614 gave 0·2685 AgBr. Br = 31·61.

$C_{10}H_{17}O_2Br$ requires Br = 32·13 per cent.

The portion boiling at 120—135° under 40 mm. pressure was repeatedly fractionated under the ordinary pressure, and in this way a quantity of a colourless oil was obtained which contained only traces of

bromine and distilled constantly at 209—210° under 733 mm. pressure On analysis:

0·1551 gave 0·3996 CO_2 and 0·1310 H_2O. C = 70·3; H = 9·4.
$C_{10}H_{16}O_2$ requires C = 71·43; H = 9·52 per cent.

This substance is *methyl tetrahydro-xylate*, the slight deficiency in the carbon and hydrogen found being due to traces of bromine which could not be entirely removed by fractional distillation. It was subsequently obtained quite free from bromine by treating methyl bromohexahydro-xylate with diethylaniline (see below). When dissolved in chloroform, methyl tetrahydro-xylate readily absorbs bromine with the formation of *methyl dibromohexahydro-xylate*.

Methyl tetrahydro-xylate (5 grams) was dissolved in carefully dried chloroform (15 grams), and after cooling the solution below 0°, dry bromine (5 grams) dissolved in chloroform (20 grams) was slowly added, the apparatus being kept in the dark during the whole operation. The bromine was almost instantaneously absorbed and only traces of hydrogen bromide were evolved. Dry air was now drawn through the solution, cooled below 0° for some hours and until the odour of chloroform had entirely disappeared, and the viscid, light yellow oil then analysed, with the following result:

0·2541 gave 0·2762 AgBr. Br = 46·25.
$C_{10}H_{16}O_2Br_2$ requires Br = 48·8 per cent.

Methyl dibromotetrahydro-xylate, $C_8H_{13}Br_2 \cdot CO_2CH_3$, is an unstable substance which, when exposed to the air at the ordinary temperature, rapidly loses hydrogen bromide and becomes dark coloured. On leaving a small quantity over paraffin wax and sulphuric acid in an exhausted desiccator for two days, it was noticed, on opening the desiccator, that much hydrogen bromide had been formed, and the oil, on analysis, was found to contain only 42·8 per cent. of bromine.

A-Tetrahydro-xylic acid (m. p. 72°).

This acid is readily obtained by the hydrolysis of its methyl ester with alcoholic potash, and in preparing it in quantity the following method was always employed.

Methyl bromohexahydro-xylate was mixed with twice its weight of diethylaniline and the mixture heated to boiling for 6 hours; the product, after cooling, was then poured into excess of dilute hydrochloric acid and the oil extracted with ether. The ethereal solution was repeatedly washed with dilute hydrochloric acid, to remove the last traces of diethylaniline, then with sodium carbonate, dried over calcium chloride, and the ether distilled off, when a light brown oil was obtained

which, after repeated fractional distillation, boiled constantly at 212—213° under 750 mm. pressure. On analysis:

0·1136 gave 0·2970 CO_2 and 0·0954 H_2O. C = 71·3; H = 9·3.
$C_{10}H_{16}O_2$ requires C = 71·4; H = 9·5 per cent.

The *methyl tetrahydro-xylate* thus obtained was hydrolysed by boiling with excess of methyl alcoholic potash for one hour, the product dissolved in water, evaporated until quite free from methyl alcohol and acidified with hydrochloric acid, when the tetrahydro-xylic acid was precipitated as an oil. This was extracted with ether (free from alcohol), the ethereal solution washed with water, dried over calcium chloride, and the ether distilled off, when a light brown oil was obtained which, after twice fractionating under diminished pressure, distilled constantly at 147—149° (20 mm.).* On analysis:

0·1524 gave 0·3915 CO_2 and 0·1236 H_2O. C = 70·1; H = 9·0.
$C_9H_{14}O_2$ requires C = 70·1; H = 9·1 per cent.

* The *methyl tetrahydro-xylate* obtained in this way is undoubtedly a mixture of the methyl esters of isomeric tetrahydro-xylic acids, and before this was discovered, the density, magnetic rotation, and refractive power of a very carefully fractionated sample of the oil were determined by W. H. Perkin, sen. The following is a brief statement of the results obtained:

d 10°/10° = 0·99556; d 15°/15° = 0·99181; d 20°/20° = 0·98823.

Magnetic rotation.

t = 11·5°; sp. rotation = 1·1380; mol. rotation, 10·682.

Refraction, d 15°/4° = 0·99097.

$\frac{\mu-1}{d}p$ – H_α = 79·025; H_β = 80·752; H_γ = 81·651.

The permanent rotation of this sample was −1·21° for 102 mm. = $[\alpha]_D$ = −1·195, and in the case of the sample prepared without diethylaniline, and analysed (see p. 351), the permanent rotation was found to be −1·24 for 100 mm. = $[\alpha]_D$ = −1·249.

Since it is unlikely that the magnetic rotation and refractive power of the two isomeric methyl tetrahydro-xylates would differ in any marked degree, it is interesting to compare the numbers obtained in the case of this unsaturated 6-membered ring with those of methyl *iso*lauronolate and methyl lauronolate, which are isomeric derivatives of an unsaturated 5-membered ring. The comparison is as follows:

	Mol. rotation.	$\frac{\mu-1}{d}p$ for H_α.
Methyl *iso*lauronolate	11·312	80·596
Methyl lauronolate	10·520	79·257
Methyl tetrahydro-xylate.....	10·682	79·025

It is certainly remarkable that whilst the numbers are so very similar in the two latter esters, they should differ so widely from those of methyl *iso*lauronolate, and further investigation may prove that there is a closer relationship between lauronolic acid and tetrahydro-xylic acid than is at present assumed to be the case. The preparation and properties of the methyl and ethyl esters of lauronolic acid will be described in a subsequent paper.

It will be seen that the analytical numbers agree exactly with those required by the formula for tetrahydro-xylic acid, and for a long time it was thought that this oily acid was a pure and single substance. However, after a considerable quantity had been left standing for some weeks in a cool place, it began to deposit crystals, and on cooling in a freezing mixture the whole became converted into a semi-solid mass which, at the ordinary temperature, liquefied again almost completely. After cooling well, the crystals were separated as far as possible from the oil by means of the pump, using a funnel surrounded by a freezing mixture, the solid mass was then left in contact with porous porcelain until quite free from oily mother liquor, and then crystallised from dilute alcohol, from which it separated in the form of glistening plates. On analysis:

0·1595 gave 0·4070 CO_2 and 0·1293 H_2O. C = 69·6; H = 9·0.
0·144 „ 0·3689 CO_2 „ 0·118 H_2O. C = 69·9; H = 9·1.
$C_9H_{14}O_2$ requires C = 70·1; H = 9·1 per cent.

This acid, which we propose to call *A-tetrahydro-xylic acid*, melts at about 72° when rapidly heated, but like many other similarly constituted acids, the melting point is much influenced by the rapidity of heating and by the slightest impurity. It is readily soluble in most organic solvents, but is almost insoluble in water; in a current of steam, it volatilises with great ease. In many of its properties, tetrahydro-xylic acid shows great similarity to lauronolic acid; like the latter, it instantly reduces permanganate in cold sodium carbonate solution, and it does not appear to be reduced by boiling with amyl alcohol and sodium (compare p. 355).*

Action of Sulphuric Acid.—When tetrahydro-xylic acid is warmed with concentrated sulphuric acid at about 80°, oxidation rapidly takes place with evolution of sulphur dioxide, and on pouring the product into water a very sparingly soluble acid separates, which, after distillation and recrystallising from dilute acetic acid, melts at 126° and shows all the properties of xylic acid. On analysis:

0·1102 gave 0·2901 CO_2 and 0·0686 H_2O. C = 71·8; H = 6·9.
$C_9H_{10}O_2$ requires C = 72·0; H = 6·7 per cent.

Even when left in contact with concentrated sulphuric acid for some days at the ordinary temperature, the solution becomes brown and smells of sulphur dioxide, and on pouring into water a crystalline acid

* Experiments which have been made with the object of reducing lauronolic acid show that this acid resists the action of reducing agents in a remarkable way, and is not even affected on treatment with sodium and alcohol. In this respect, it differs from *iso*lauronolic acid, which is comparatively easily reduced to dihydro*iso*-lauronolic acid (compare footnote, p. 352).

separates which, after purification, melts at 126° and evidently consists of xylic acid.

Anilide of Tetrahydro-xylic Acid.—In order to determine whether a separation of the constituents of the oily mixture of tetrahydro-xylic acid was possible by conversion into the anilides and fractional crystallisation, 5 grams of the oily acid were digested with 15 grams of aniline for 2 days. The brown product was poured into dilute hydrochloric acid, the oily precipitate extracted with ether, the ethereal solution washed first with dilute hydrochloric acid, and then with dilute potash solution, dried with calcium chloride, and the ether distilled off. The residue quickly solidified, and, after leaving it in contact with porous porcelain for a short time, the almost colourless mass was easily purified by recrystallisation from light petroleum (b. p. 80—100°), from which it separated in satiny crystals melting at 131—132°. On analysis:

0·1930 gave 10·8 c.c. nitrogen at 24° and 761 mm. N = 6·2.

$C_{15}H_{19}ON$ requires N = 6 per cent.

This substance being the anilide of an unsaturated acid, could not be hydrolysed with strong acids, and in attempting the hydrolysis with alcoholic potash it was found that this reagent had apparently no action, as after boiling for two days almost the whole of the substance was precipitated unchanged on the addition of water. When, however, the anilide was heated in a sealed tube with strong alcoholic potash at 170° for 10 hours, some decomposition had taken place, but on evaporating off the alcohol and adding water, more than half of the unchanged anilide separated out. After filtering, the alkaline liquid was acidified and the oily acid extracted with ether in the usual way, when the ethereal solution on evaporating deposited an oil which, on standing over sulphuric acid in a vacuum, soon solidified to crystals melting at 66—68°, showing that the substance of melting point 131—132° is the *anilide* of *A-tetrahydro-xylic acid.*

In preparing the anilide in this way, any acid which had remained unchanged was extracted by shaking the ethereal solution with potash as described above. Since, then, the original oily acid was a mixture, it is evident that if, as was the case, a large proportion of A-tetrahydro-xylic acid had been removed as anilide, the remainder should consist principally of the other isomeride. The acid was isolated from the alkaline washings and fractionated, when the whole quantity passed over at 253° as a colourless oil, which became semi-solid in a freezing mixture, and behaved very much like the original acid before treatment with aniline. Apparently, then, both the isomerides are converted into anilides by boiling with aniline, but the anilide melting at 132° evidently crystallises with greater facility, and is, therefore,

more readily obtained in a state of purity. We did not carry this investigation further because, even if we had succeeded in separating the anilides by crystallisation, they are hydrolysed with such difficulty that the process could only be used, at the best, for the preparation of small quantities of the two acids.

Action of Sodium and Amyl Alcohol on the Mixed Tetrahydro-xylic Acids.—In this attempt to reduce the tetrahydro-xylic acids, 30 grams of the mixed acids, as obtained by the hydrolysis of methyl tetrahydro-xylate (p. 352), were dissolved in 2 litres of amyl alcohol in a large, round-bottomed flask connected with a wide condenser.

The solution was heated to boiling, the flame removed, and then sodium (40 grams) dropped in in three portions, and sufficiently quickly to keep the liquid boiling as rapidly as possible. As soon as the reaction had slackened, heat was applied, and when the sodium had dissolved, sufficient dilute hydrochloric acid was added to render the product distinctly acid; the alcohol layer was then separated, and distilled from a retort until the temperature rose to 120—125°. The treatment with sodium was repeated exactly as before, and four times in all, water was then added, and after the aqueous extract had been separated, the bulk of the amyl alcohol was removed by distillation and the remainder by distillation in steam. The aqueous residue in the steam distillation flask was combined with the aqueous extract, and the whole, after saturating with carbon dioxide, oxidised at 0° with permanganate, when it was found that a large amount of the oxidising agent was required before the colour remained permanent.

After standing for 1 hour at 0°, the excess of permanganate was removed by adding sodium sulphite, the whole boiled, filtered, the filtrate concentrated, acidified, and distilled in steam as long as oily drops passed over.

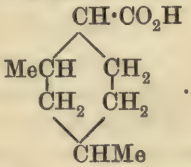
The distillate was saturated with ammonium sulphate and extracted several times with ether; the ethereal solution was then dried over calcium chloride and evaporated, when from 60 grams of tetrahydro-xylic acid about 4 grams of an oily acid were obtained, almost the whole of which, on distillation, passed over at 253—255°. On analysis:

0·1225 gave 0·3112 CO_2 and 0·1129 H_2O. C = 69·3; H = 10·2.

$C_9H_{16}O_2$ requires C = 69·2; H = 10·2 per cent.

There can scarcely be a doubt that this acid is a mixture of the stereoisomeric modifications of hexahydro-xylic acid, but it is produced in such small quantity that we were unable to effect a separation of its constituents.

The Action of Aluminium Chloride on iso*Lauronolic Acid. Formation of* cis- *and* trans-*Hexahydro-xylic Acids,*



When aluminium chloride is left in contact with a chloroform solution of camphoric anhydride for several weeks, the product of the reaction differs in a marked way from that obtained when the mixture is worked up after standing for a few hours, as described on p. 341.

The chief difference is that almost the whole of the *iso*lauronolic acid has disappeared, and in its place large quantities of the two stereoisomeric modifications of hexahydro-xylic acid are found ; these must, apparently, have been produced by the long-continued action of the aluminium chloride on the *iso*lauronolic acid.

In investigating this decomposition, several quantities of the mixture of camphoric anhydride, chloroform, and aluminium chloride, prepared exactly as described on p. 341, were allowed to stand in most cases for 6 weeks, and then worked up in the same way as before. It was noticed, in the first place, that the amount of the lactones of hydroxyhexahydro-xylic acid was approximately the same as when the mixture was allowed to stand only a short time. On acidifying the potash extract, however, instead of the usual ochre-coloured, crystalline precipitate of crude *iso*lauronolic acid, an oily acid was thrown down, which, after extracting with ether and distilling off the ether, remained as a dark brown, viscid oil.

This oil was dissolved in dilute ammonia, and subjected to distillation with steam until a sample of the distillate, on acidifying, remained clear, when it was noticed that the residue in the distilling flask, after cooling, solidified to a brown button as before. The alkaline distillate was acidified and extracted with ether, and after the ethereal solution had been dried over calcium chloride and evaporated, a large quantity of a yellow oil was left, amounting to about 25 per cent. of the camphoric anhydride employed. As this oily acid was found to contain a small quantity of a neutral oil, it was dissolved in ether, the ethereal solution extracted with dilute potash, the acid reprecipitated, and after extraction fractionated under reduced pressure (28—30 mm.).

The acid began to boil at 152°, and between this temperature and 160° the whole quantity passed over as a colourless oil which, on refractionation, distilled for the most part constantly at 155—156° under the same pressure. On analysis :

0·1761 gave 0·4483 CO_2 and 0·1565 H_2O. C = 69·42; H = 9·9.
$C_9H_{16}O_2$ requires C = 69·23; H = 10·25 per cent.
$C_9H_{14}O_2$ „ C = 70·12; H = 9·10 „

This analysis showed that the oil which boiled so constantly was not pure, but evidently consisted of large quantities of an acid, $C_8H_{15}\cdot CO_2H$, mixed with smaller quantities of an acid, $C_8H_{13}\cdot CO_2H$, a view borne out by the fact that the oil when dissolved in sodium carbonate was capable of reducing a good deal of permanganate in the cold. In order to remove the unsaturated constituent, the whole was dissolved in sodium carbonate and, after adding ice, treated with permanganate until the colour was no longer destroyed.

The filtrate and washings from the manganese precipitate were evaporated to a small bulk, the acid reprecipitated and subjected to distillation in steam, when the residue in the distilling flask, on standing, deposited long, yellow needles of *iso*lauronic acid, showing that the unsaturated constituent of the original oil consisted, in part, at all events, of *iso*lauronolic acid.

The distillate was extracted with ether in the usual way, and the acid again fractionated, when almost the whole quantity distilled constantly at 149—150° under 20—25 mm. pressure, but as it was still not quite stable towards permanganate, the treatment with this reagent was again resorted to, with the difference that the oxidation was carried out at the ordinary temperature instead of at 0°. After this second treatment, the acid, which now contained no trace of unsaturated impurity, distilled completely at 154—157° under 30 mm. pressure as a colourless oil which, on standing, soon began to deposit crystals.

The whole was allowed to stand for 10 days in an ice chest; the crystals were then rapidly collected on the pump, left in contact with porous porcelain until quite dry, and finally recrystallised from dilute acetic acid, from which solvent the acid separated in long, glistening needles melting at 73—75°. On analysis:

0·1396 gave 0·3525 CO_2 and 0·1276 H_2O. C = 68·9; H = 10·2.
0·1531 „ 0·3883 CO_2 „ 0·1410 H_2O. C = 69·2; H = 10·2.
$C_9H_{16}O_2$ requires C = 69·2; H = 10·2 per cent.

This acid is a remarkably stable substance, since it may be boiled with nitric acid for some time without being appreciably oxidised, and on cooling it crystallises out unchanged in needles which melt sharply at 75°.

The *silver* salt was precipitated on adding silver nitrate to a nearly neutral solution of the ammonium salt as a white, gelatinous mass, which, however, on stirring and warming, became crystalline. It was collected, washed well, dried at 100°, and analysed:

0·1165 gave 0·1761 CO_2, 0·0593 H_2O, and 0·0482 Ag. C = 41·2; H = 5·6; Ag = 41·3.

$C_9H_{15}O_2Ag$ requires C = 41·1; H = 5·7; Ag = 41·1 per cent.

For a long time, no clue to the constitution of this acid, of melting point 75°, could be obtained, but ultimately the investigation of its behaviour, first with bromine and then with alcoholic potash, made it probable that it was trans-*hexahydro-xylic acid.* On comparing the properties of this acid with those of a sample of hexahydro-xylic acid prepared by Bentley and Perkin (*loc. cit.*) by the reduction of xylic acid, they were found to be identical, since on mixing equal quantities of the two different preparations, no alteration could be observed in the melting point. It is clear, therefore, that one of the acids produced by the action of aluminium chloride on *iso*lauronolic acid is trans-*hexahydro-xylic acid.*

The experiment which led us to suspect the identity of this acid was the following.

The acid of melting point 75° (9 grams) was mixed carefully with the calculated quantity of phosphorus pentachloride (12 grams), and after the reaction, which commenced at once, had ceased, the mixture was heated for 15 minutes on the water-bath. Bromine (10 grams) was then added to the well cooled product, and the whole heated on the water-bath in a reflux apparatus until the colour of the bromine had disappeared and the evolution of hydrogen bromide had almost ceased. The liquid was then gradually poured into three times its volume of well cooled methyl alcohol and allowed to stand over night. On the addition of much water, a heavy, light brown oil separated which was extracted with ether, the ethereal solution was then well washed with dilute sodium carbonate, dried over calcium chloride, and the ether distilled off, when a light yellow oil (17 grams) was obtained which distilled almost completely at 143—146° under 35—38 mm. pressure. On analysis:

0·2780 gave 0·2091 AgBr. Br = 32·0.

$C_{10}H_{17}O_2Br$ requires Br = 32·1 per cent.

This substance is *methyl α-bromohexahydro-xylate,* $C_8H_{14}Br{\cdot}CO_2CH_3$, since on hydrolysis with alcoholic potash it yields *tetrahydro-xylic acid.*

The pure methyl ester was rapidly poured into a large excess of strong boiling alcoholic potash, and after the vigorous reaction had subsided the whole was boiled for 15 minutes, mixed with water, and evaporated on the water-bath with the frequent addition of water in order to ensure the removal of the last traces of alcohol. On acidifying the alkaline solution with hydrochloric acid, an oily acid separated, but this rapidly solidified; it was extracted with ether, and the ethereal solution, after drying, evaporated, when a solid residue remained

which, on distillation, passed over at 254—255° as a colourless oil solidifying almost immediately to a hard, crystalline cake. The solid mass was spread on porous porcelain to remove traces of oily impurity, and then crystallised from dilute alcohol, from which it separated in colourless needles melting sharply at 106°. On analysis:

0·1277 gave 0·3265 CO_2 and 0·1072 H_2O. C = 69·7; H = 9·3.
0·1271 „ 0·3268 CO_2 „ 0·1060 H_2O. C = 70·1; H = 9·2.
$C_9H_{14}O_2$ requires C = 70·1; H = 9·1 per cent.

This acid is identical with the *tetrahydro-xylic acid* which is produced by the reduction of xylic acid by means of sodium and amyl alcohol. In their paper on the formation of this acid, Bentley and Perkin (*loc. cit.*) give the melting point as 103°, but this is too low, since the original specimen, prepared by the reduction of xylic acid, after several times recrystallising, was found to melt at 106°.

On intimately mixing equal quantities of this latter specimen and the acid prepared from methyl bromohexahydro-xylate, there was no alteration in the melting point.

cis-*Hexahydro-xylic Acid.*—The oil separated from the crystals of *trans*-hexahydro-xylic acid in the manner described in the last section, deposited, on standing for some months in an ice chest, a further quantity of the same acid, and after filtering from the crystals the oily filtrate became semi-solid on placing in a freezing mixture of ice and salt, but rapidly and completely melted as soon as it was taken out of the freezing mixture. This behaviour suggested that the oily acid was a mixture of two isomerides and as, in spite of many experiments, a further separation by freezing was not successful, an attempt was made to effect this separation by converting the mixture of acids into the amides and subjecting these to fractional crystallisation. The oily acid (100 grams) was mixed with a slight excess of phosphorus pentachloride, in a large flask connected with a reflux apparatus and, after the vigorous action had subsided, the whole was heated in the water-bath for 15 minutes and when cold poured in a thin stream into strong aqueous ammonia (saturated below 0°).

The crystalline amides which separated were collected on the pump, washed with ammonia, dried, ground to a fine powder, and extracted with ether, by which means oily impurity was removed and a perfectly dry, crystalline mass resulted.

This amide, which had no definite melting point and was evidently a mixture, was submitted to a series of fractional crystallisations, first from much water and then from alcohol, and in this way it was separated into a sparingly soluble amide melting at 188—189° and a more soluble, and obviously less pure, fraction melting at 120—140°.

The amide melting at 188—189° was analysed, with the following results:

0·2325 gave 19·2 c.c. nitrogen at 24° and 760 mm. N = 9·2.
$C_9H_{17}ON$ requires N = 9·0 per cent.

When boiled with concentrated hydrochloric acid, this amide was hydrolysed and the oily acid which floated on the hot liquid solidified on cooling to crystals which, without further purification, melted at 72°. It is obvious, therefore, that this amide is the amide of *trans*-hexahydro-xylic acid.

The crude amide melting at 120—140° was subjected to upwards of 50 fractional crystallisations from water, and ultimately a substance was obtained which crystallised in long, slender, silky needles and melted, not quite sharply, at 140—142°. On analysis:

0·2095 gave 17 c.c. nitrogen at 20° and 754 mm. N = 9·2.
$C_9H_{17}ON$ requires N = 9·0 per cent.

This amide, which we believe to be the amide of cis-*hexahydro-xylic acid*, dissolves readily in warm concentrated hydrochloric acid, and, on boiling, decomposition soon sets in, and oily drops of the acid appear rapidly on the surface of the liquid. The acid was extracted with ether, the ethereal solution dried over calcium chloride, and after distilling off the ether the oily residue fractionated, when almost the whole quantity passed over at 250—252°. On analysis:

0·1460 gave 0·3694 CO_2 and 0·1353 H_2O. C = 69·0; H = 10·3.
$C_9H_{16}O_2$ requires C = 69·2; H = 10·2 per cent.

cis-*Hexahydro-xylic acid*, obtained in this way, is an oil which, even when cooled below −10° and stirred with a crystal of the *trans*-acid, shows no signs of crystallising. When it is remembered that all the *trans*-acid which could be separated by freezing had already been carefully removed from the oily mixture of the hexahydro-xylic acids, and that during the conversion into and subsequent fractional crystallisation of the amides a further considerable quantity of *trans*-acid was again removed, it is unlikely that the *cis*-acid which we obtained could have contained more than traces of the *trans*-acid. At the same time, we do not suggest that the *cis*-acid was quite pure, and it is therefore possible that the melting point of its amide may not be exactly that given above.

The experiments on the substances described in this paper are being continued, and it is hoped that the results will soon be ready for communication to the Society. We desire to state that much of the

very heavy expense which was necessary in carrying out these experiments has been met by repeated grants from the Royal Society.

Our thanks are also due to Mr. J. Yates for undertaking the preparation of much of the material necessary for this research, and for carrying out several of the analyses.

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THE ACTION OF ALUMINIUM CHLORIDE ON CAMPHORIC ANHYDRIDE. PART II.

BY

W. H. PERKIN, JUN.,

AND

J. YATES.

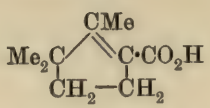
From the Transactions of the Chemical Society, 1901. Vol. 79.

CXLV.—*The Action of Aluminium Chloride on Camphoric Anhydride. Part II.*

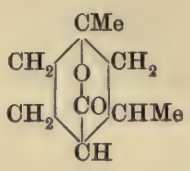
By W. H. Perkin, jun., and J. Yates.

In the first part of this paper, published a short time ago (Lees and Perkin, this vol., 332), it was shown that when camphoric anhydride, dissolved in chloroform, is treated in the cold with aluminium chloride, the camphor molecule undergoes a series of remarkable molecular changes.

The substances formed during this decomposition and described in the first paper were *so*lauronolic acid,

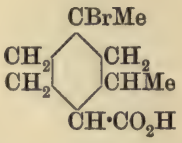


and a mixture of isomeric lactones, which, since they are readily converted into xylic acid on oxidation with sulphuric acid, were recognised as stereoisomeric modifications of the lactone of hydroxyhexahydro-xylic acid,



By hydrolysing the mixed lactones we succeeded, in a way described in detail in that paper, in isolating two well characterised stable hydroxyhexahydro-xylic acids melting at 160° and 113° respectively, which we called simply A and B, since we had no means of determining their configurations. When distilled, these acids were converted into the corresponding lactones with elimination of water, the lactone of the A-acid melted at 55°,* and that of the B-acid at 44°.

We have since further examined these two hydroxy-acids and their lactones and find that the A-acid or its lactone, when treated with fuming hydrobromic acid, is converted into *A-bromohexahydro-xylic acid*,



which melts at 133°, whereas the B-hydroxy-acid and its lactone, under similar conditions, yield *B-bromohexahydro-xylic acid* melting at 126°.

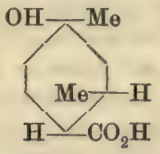
In our earlier experiments, several results were obtained which seemed to indicate that the lactone mixture obtained by the action of aluminium chloride on camphoric anhydride did not consist entirely of the two lactones of A- and B-hydroxyhexahydro-xylic acid, but contained other isomeric lactones, which we were at that time unable to isolate. Since then, by experimenting with large quantities of material, this

* This lactone was described as an oil, but it subsequently solidified,

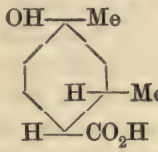
suspicion has been confirmed and we have now been able to identify all the constituents of the mixture.

The two hydroxy-acids, A and B, are characterised by remarkable stability, since, although they contain the hydroxyl and carboxyl groups in the δ-position, they are not converted into their lactones even by prolonged boiling with water, and it was found necessary, in order to prepare these lactones, to submit the acids to dry distillation.*

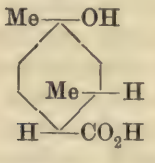
In order to explain this remarkable stability, we suggested in the earlier paper that the two hydroxy-acids, A and B, were probably the *trans*-modifications,



and



The corresponding *cis*-modifications,



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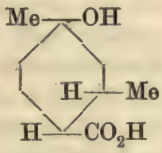
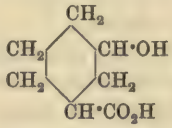
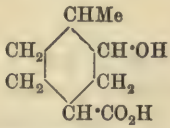


might be expected to exhibit much less stability, and be converted into their lactones when their salts are acidified, as is the case with the δ-hydroxy-acids in the fatty series.

* Somewhat similar cases of stable ring hydroxy-acids have already been observed. Thus, the hydroxy*cyclo*hexanecarboxylic acid of the formula



which Einhorn (*Annalen*, 1896, **291**, 298) prepared by reducing *m*-hydroxybenzoic acid, is quite stable although it is a γ-hydroxy-acid. Again, Tiemann and Semmler (*Ber.*, 1895, **28**, 2143) describe as stable the γ-hydroxyhexahydro-*p*-toluic acid of the formula:



Both these acids are probably *trans*-modifications.

The existence of *cis*- and *trans*-isomerism in the case of ring-acids containing the

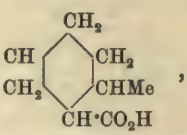
By making use of these differences in stability we have now succeeded in showing that the mixed lactones obtained by the action of aluminium chloride on camphoric anhydride contain, not only the lactones of the *trans*-A- and B-hydroxyhexahydro-xylic acids, but also the corresponding *cis*-lactones. The process employed in separating the latter is briefly as follows:

The mixed lactones are first converted into the hydroxy-acids by hydrolysis and these then submitted to distillation in steam; in this way, the *cis*-hydroxy-acids are converted into lactones which pass over with the steam, whereas the *trans*-acids remain for the most part unchanged in the distilling flask, so that by repeating this process an almost complete separation is possible. The last traces of *trans*-acids are removed by hydrolysing the lactones and allowing the hydroxy-acids to stand for a few days, when the *cis*-modifications are spontaneously converted into lactones, which are separated from any traces of *trans*-hydroxy-acids by treatment with sodium carbonate. In this way, more than 100 grams of oil were obtained, which distilled constantly at 145° under 25 mm. pressure, and, like the *trans*-lactones, yielded xylic acid when treated with sulphuric acid; there can therefore be no doubt that it consisted of the *cis*-lactones of hydroxyhexahydro-xylic acid.

Further examination showed that this oil contains two lactones (one, however, only in extremely small quantity), since when treated with fuming hydrobromic acid the oil yields a solid product which, when crystallised from light petroleum, may be separated into a small quantity of a very sparingly soluble C-bromohexahydro-xylic acid melting at 137° and a large quantity of the more soluble D-bromohexahydro-xylic acid, which melts at 130°. At first it was thought that the two bromo-acids, A and C, melting at 133° and 137°, and the two B, and D, melting at 128° and 130° were identical, but investigation showed that this is not the case.

If, for example, the first two are intimately mixed, the mixture melts at about 100° and a mixture of the two latter was found to melt at about 105°, and again, the four bromo-acids differ in their behaviour with sodium carbonate: a point which will be discussed at a later stage.

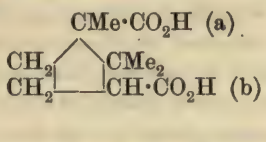
groups CHMe and $CH{\cdot}CO_2H$ has already been observed. Thus, hexahydro-*o*-toluic acid,



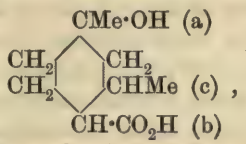
exists in well-defined *cis*- and *trans*-modifications (Goodwin and Perkin, Trans., 1895, **67**, 121).

It is therefore evident that there are four distinct bromo-acids, $C_9H_{15}O_2Br$, two *cis* and two *trans*, and this agrees with the assumption that the hydroxy-acids, $C_9H_{15}O_2{\cdot}OH$, from which they are derived, are stereoisomeric modifications of hydroxyhexahydro-xylic acid, and that the bromo-acids are therefore stereoisomeric bromohexahydro-xylic acids: this will be evident from the following considerations.

If the formula of camphoric acid is compared with that of hydroxy-hexahydro-xylic acid,



Camphoric acid.



Hydroxyhexahydro-xylic acid.

it will be seen that not only are the two asymmetric carbon atoms in the camphoric acid (marked a, b) present in the hydroxyhexahydro-xylic acid, although in a somewhat altered form, but that in the formation of the latter acid from the former a new asymmetric carbon (marked c) has been created: in other words, hydroxyhexahydro-xylic acid contains *three* asymmetric carbon atoms. In order to discuss this point, we may conveniently select the four bromo-acids A, B, C, and D, and it may be stated at once that experiment has shown that these are all inactive and that, therefore, racemisation must have taken place in their formation from the strongly dextrorotatory camphoric anhydride. In the case of a substance containing three asymmetric carbon atoms a, b, c, the possible combinations, using the signs + and − are:

+ a − a	+ a − a	+ a − a	− a + a
+ c − c	− c + c	− c + c	− c + c
+ b − b	+ b − b	− b + b	+ b − b
1 2	3 4	5 6	7 8

that is to say, there are four possible externally compensated combinations, 1 : 2, 3 : 4, 5 : 6, and 7 : 8, and it is highly probable that the four bromo-acids, A, B, C, and D, and their corresponding hydroxy-acids, are these combinations. Unfortunately, it is not possible at this stage to assign to *each* modification its particular configuration. We may, however, select the combination [+a−c−b, −a+c+b] for C, in which case D will be [−a−c+b, +a+c−b], and the acids A and B will be represented by [+a+c+b, −a−c−b] and [+a−c+b, −a+c−b], but which of these symbols belongs to A, and which to B, must be left an open question.

In connection with this question of the introduction of a new asymmetric carbon atom into a molecule containing already one or more such carbon atoms, we may perhaps be allowed to call attention to the

following very interesting aspect of the subject, since it arises directly from our experimental work.

It has already been stated that the results briefly described above leave little room for doubting that during the conversion of *d*-camphoric acid the change proceeds in such a way as to yield the four externally compensated hydroxyhexahydro-xylic acids, to which only the configurations given on page 1377 can be assigned. It thus follows that the camphor residue has, during the treatment with aluminium chloride, undergone racemisation in a manner similar to, although probably more complete than, that observed by Kipping and Pope (Trans., 1897, **71**, 956) to occur on sulphonating camphor; and whilst in the latter case the complex $+a+b$ became converted into $-a-b$, in the case now described the other two complexes, $+a-b$ and $-a+b$, are also produced at some stage during the series of reactions. The formation of a third asymmetric carbon atom in addition to the two already present results in the ultimate production of all eight possible configurations of the substance containing three dissimilar asymmetric carbon atoms.

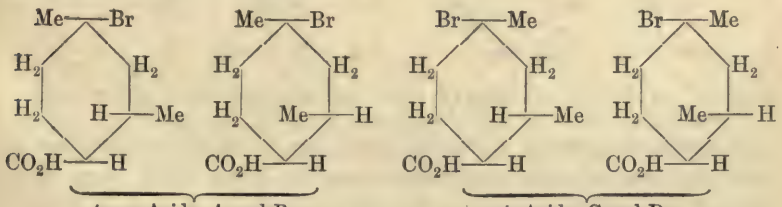
Quite recently (Cohen and Whiteley, Proc., 1900, **16**, 212; Kipping, *ibid.*, 226), the question has again been opened as to whether in converting an optically active substance containing *n*-asymmetric carbon atoms into one containing $n+1$ such atoms, the configuration of the *n*-asymmetric carbon atoms originally present exercises a directive influence on the configuration of the new asymmetric carbon atom. This question seems to have been answered in the affirmative by Fischer's work, and more especially by his observation that *d*-mannose, which contains four asymmetric carbon atoms, gives an almost quantitative yield of *d*-mannoheptonic acid (*Ber.*, 1889, **22**, 370), which contains five asymmetric carbon atoms in the molecule. A number of well-known facts leading to the same conclusion are available and the work now described also points in the same direction. Thus, it is well known that on brominating succinic acid two optically inactive dibromosuccinic acids are obtained in different quantities, the isomeride (*iso*dibromosuccinic acid) produced in much the smaller amount having the configuration $[+a+a,-a-a]$, whilst ordinary dibromosuccinic acid is the internally compensated compound having the configuration $[+a-a]$. Since monobromosuccinic acid containing one asymmetric carbon atom is first produced and on further bromination yields more internally than externally compensated dibromosuccinic acid, it follows that the presence of one asymmetric carbon atom in this case causes the second to assume, by preference, the opposite configuration to the first. The literature concerning the tartaric acids reveals similarly convincing proofs of the same proposition. The possibility of drawing, from the behaviour of optically

inactive substances, sound conclusions as to the directive influence exerted by the configuration of asymmetric carbon atoms already existent in the substance upon that of others ultimately produced, seems hitherto to have been overlooked. In the formation of the hydroxyhexahydro-xylic acids with three asymmetric carbon atoms from camphoric acid containing only two, we show that the four externally compensated isomerides produced are formed in widely different proportions, which may be roughly stated to be as follows: A, 12 per cent.; B, 5 per cent.; C, 3 per cent.; D, 80 per cent. Although we are unable at present to definitely distribute the four pairs of possible configurations amongst these four acids, the fact that these acids are formed in different quantities is convincing proof that the configurations of the two original asymmetric carbon atoms have exercised a directive influence on the configuration of the carbon atom, which becomes asymmetric during the action of the aluminium chloride.

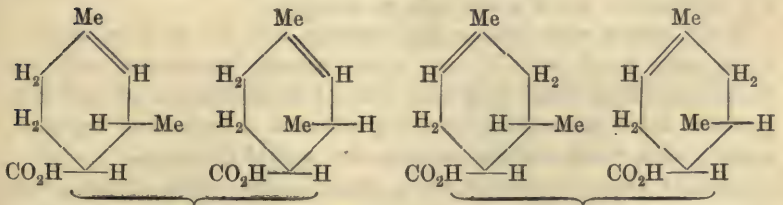
When the four bromo-acids, A, B, C, D, are boiled with sodium carbonate, they are all decomposed with elimination of hydrogen bromide and formation of tetrahydro-xylic acids,

$$C_9H_{15}O_2Br = C_9H_{14}O_2 + HBr,$$

and according to theory, four different externally compensated acids should be formed in this way, as will be seen at once if the bromo-acids are represented graphically and the corresponding tetrahydro-xylic acids written underneath.



Bromohexahydro-xylic acids.



Tetrahydro-xylic acids.

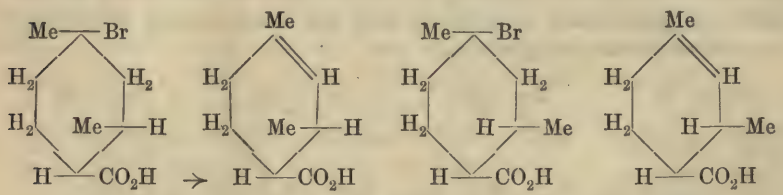
As in this change (elimination of hydrogen bromide), only one of

the three asymmetric carbon atoms in the bromohexahydro-xylic acids disappears, each of [the unsaturated acids formulated above still contains two asymmetric carbon atoms and is an externally compensated compound; the optical relationship of these four racemic compounds may therefore be expressed by the same signs as before, omitting that given to the >CMeBr-group. The tetrahydro-xylic acid, C, will therefore be [−c−b, +c+b], D will be [−c+b, +c−b], and A and B will be either [+c+b, −c−b] or [−c+b, +c−b].

The actual results of the experiments on the behaviour of the four bromo-acids with sodium carbonate show that the three bromo-acids, A, B, and D, give three distinct tetrahydro-xylic acids, A, B, and D, which melt at 80°, 68°, and 87° respectively, but in the case of the bromo-acid, C, the material at our disposal was so small that we were unable to purify the acid formed sufficiently to determine its melting point accurately; most probably it is the fourth isomeride indicated by theory.

There is, however, at present no proof of the actual position of the double linkings in the tetrahydro-xylic acids, and the formulæ given above are only intended as examples of the direction in which elimination of hydrogen bromide may possibly take place.

It is clear that the relationship, for example, between the *cis*-bromo-acids, C and D, and their corresponding tetrahydro-xylic acids might equally well be written thus:

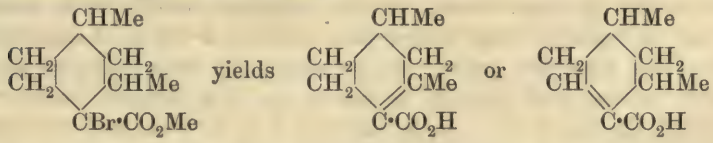


In order, if possible, to obtain some clue as to the constitution of these unsaturated acids, experiments (see pp. 1388, 1393) were instituted on the oxidation of the tetrahydro-xylic acids, A and D, but the results obtained with the small quantities of these acids available were not sufficient to throw much light on this point.

When treated with fuming hydrobromic acid, the three tetrahydro-xylic acids A, B, and D are quantitatively reconverted into the bromo-acids from which they were derived by elimination of hydrogen bromide, the bromine atom becoming attached in each case, therefore, to the tertiary carbon atom carrying the methyl group.

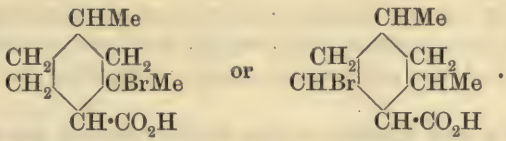
Another characteristic of these acids is that when warmed with sulphuric acid at 80° they are rapidly oxidised to xylic acid and, indeed, this change takes place at the ordinary temperature if the solution in sulphuric acid is allowed to stand for some days.

During the course of a series of experiments on the reduction of xylic acid by means of sodium and *iso*amyl alcohol, Bentley and Perkin (Trans., 1897, 71, 173) obtained a tetrahydro-xylic acid which melts at 107° and is isomeric with the tetrahydro-xylic acids, A, B, and D, described in the present paper. That this acid is either Δ^1- or Δ^6-tetrahydro-xylic acid is conclusively proved by the fact that it is formed from methyl α-bromohexahydro-xylate by hydrolysis and elimination of hydrogen bromide.



In order to obtain further evidence in support of the assumption that the acids A, B, and D are tetrahydro-xylic acids, we decided to further examine this acid of melting point 106°, and as the result of our experiments we find in properties and behaviour with reagents it shows a quite striking similarity to the acids A, B, and D.

Thus, for example, when heated with sulphuric acid, it is readily oxidised to xylic acid, and it combines readily with hydrogen bromide, yielding a new bromohexahydro-xylic acid which melts at 127° and the constitution of which is doubtless represented by one of the formulæ,



It is remarkable that the five bromohexahydro-xylic acids described in this paper should all melt between 127° and 137°, and that the three tetrahydro-xylic acids, A, B, and D, should all melt close together and be so very similar in properties. The impossibility of readily distinguishing between these different isomeric modifications has very greatly added to the difficulties of this reseach.

Experimental.

Separation of the Lactones produced by the action of Aluminium Chloride on Camphoric Anhydride.

In the introduction, it was stated that a new method for separating these lactones had been worked out, which gives much more satisfactory results than that described in the previous paper and is especially convenient for the rapid isolation of the *cis*-lactones. This method is as follows:

The solution of the camphoric anhydride in chloroform is first treated with aluminium chloride exactly as described in the previous paper, and after separating the *iso*lauronolic acid by means of potash, the chloroform solution of the lactones is distilled from the water-bath until as much chloroform as possible has been removed. The dark-brown residue, which often still contains 50 per cent. of its weight of chloroform, is fractionated twice under reduced pressure, when the whole passes over at 170—180° (80 mm.) as a colourless oil, the weight of which from 1 kilo. of camphoric anhydride is usually about 130 grams. The mixed lactones from 2 kilos. of camphoric anhydride were now treated on the water-bath with sufficient moderately concentrated barium hydroxide to just dissolve them, the solution filtered from a small quantity of a dark-coloured impurity, the filtrate acidified, saturated with calcium chloride, and extracted at least 20 times with pure ether. The ethereal solution was then evaporated and the residual thick oil submitted to distillation in a rapid current of steam (*a*). When oil ceased to come over with the condensed water, the distillate was saturated with ammonium sulphate, repeatedly extracted with ether, and after evaporating off the ether, the oily lactone mixture was again boiled with barium hydroxide until dissolved: the solution was then cooled to 60°, acidified with excess of hydrochloric acid, and kept at 60° for 5 minutes.

After saturating with calcium chloride, the whole was extracted twenty times with ether; the ethereal solution was then well washed with strong sodium carbonate (*b*), dried over calcium chloride, evaporated, and the residual colourless oil distilled under reduced pressure.

During the first distillation, the whole quantity passed over at 174—177° (80 mm.) and weighed 120 grams; on distilling again, more than 100 grams passed over between 175° and 176° under the same pressure. On analysis:

0·1176 gave 0·3017 CO_2 and 0·099 H_2O. C = 70·0; H = 9·3.

$C_9H_{14}O_2$ requires C = 70·1; H = 9·1 per cent.

This lactone was slightly lævorotatory, the observed rotation in a 100 mm. tube being only $-4·24°$.

In order to make quite sure that this oil was quite free from even traces of the lactones of the *trans*-acids A and B, it was again dissolved in baryta water, and the solution, after standing until quite cold, acidified with excess of hydrochloric acid, care being taken that the temperature did not rise above 15°. The whole was then allowed to stand for 24 hours, when it was noticed that the oily layer, which at first was quite thick, had become much more mobile. After extracting as usual with ether, the ethereal solution was washed repeatedly with

sodium carbonate (*c*), dried over calcium chloride, and evaporated, when 90 grams of a lactone were obtained which distilled constantly at 145° under 25 mm., and at 255° under 760 mm. pressure, and had a rotation in a 100 mm. tube of −5·3°. Experiment showed that further treatment with baryta, exactly as just described, did not alter this rotation or the other physical constants of the oil. It was therefore clear that it was now quite free from the lactones of the *trans*-A- and B-acids, and consisted of the lactones of the *cis*-acids only. In this condition, it was employed in the experiments described in this paper. On analysis, the following numbers were obtained :

0·1646 gave 0·4237 CO_2 and 0·1376 H_2O. C = 70·2 ; H = 9·3.
$C_9H_{14}O_2$ requires C = 70·1 ; H = 9·1 per cent.

The density and magnetic rotation of this oil were determined by W. H. Perkin, sen., with the following results :

Density determinations: *d* 10°/10° = 1·0503 ; *d* 15°/15° = 1·0471 ; *d* 20°/20° = 1·0441.

Magnetic rotation.

t.	Sp. rotation.	Mol. rotation.
15°	1·0562	8·632

These numbers differ considerably from the previous determinations made with the mixture of *cis*- and *trans*-lactones, the density was then at 10°/10° = 1·0606 and the magnetic rotation 8·200, and they naturally differ still more for the values found for the lactone of the *trans*-acid A (see p. 1390), which are as follows : Density, *d* 10°/10° = 1·0640 ; magnetic rotation, 8·174.

Action of Sulphuric Acid on the cis-*Lactones. Formation of Xylic Acid.*—The oily lactone just described dissolves in concentrated sulphuric acid with development of a good deal of heat, and if the solution is heated at 80° it rapidly darkens and much sulphur dioxide is evolved. After heating for 15 minutes, the product was poured into water and allowed to stand overnight ; the dark precipitate was then collected, dissolved in sodium carbonate, and boiled with purified animal charcoal. On acidifying, a rather dark coloured crystalline mass separated, and this, after drying, was distilled and the distillate crystallised from dilute acetic acid, when almost colourless crystals separated which melted at 124—125° and consisted of *xylic acid*, $C_6H_3(CH_3)_2 \cdot CO_2H$. On analysis :

0·1298 gave 0·3422 CO_2 and 0·0794 H_2O. C = 71·9 ; H = 6·8.
$C_9H_{10}O_2$ requires C = 72·0 ; H = 6·7 per cent.

Separation of the Substances Removed during the Purification of the cis-*Lactones.*

During the purification of the *cis*-lactones, as described in the previous section, more than half of the original mixture of *cis*- and *trans*-lactones was removed during the steam distillation and afterwards by the repeated extractions with sodium carbonate. The investigation of this material was carried out briefly as follows. The sodium carbonate extract *b* (p. 1382) was acidified, saturated with calcium chloride, and repeatedly extracted with ether; the ethereal solution, after carefully drying over calcium chloride and evaporating to a small bulk, yielded, on standing, 17 grams of colourless crystals, which, after recrystallisation from ether, melted at 158—160° and consisted of pure A-hydroxyhexahydro-xylic acid (this vol., p. 345).

The ethereal mother liquors of these crystals deposited, on spontaneous evaporation, several crops of crystals which, when left in contact with porous porcelain to remove oily impurity, became hard and colourless, and on subsequently recrystallising from ether, yielded further quantities of the A-acid.

The total amount of pure A-acid obtained from this sodium carbonate extract was 27 grams.

It is rather remarkable that such considerable quantities of the A-acid should be found at this place, since its presence here shows that it must have been carried over during the steam distillation, yet in the previous paper (p. 345) it was shown that the pure A-acid is not volatile as such with steam, nor is it converted into its volatile lactone under these conditions. It therefore follows that in the present case its volatility must be due to the presence of the lactones of the *cis*-acids, which carry it over during the steam distillation.

The sodium carbonate extract *c* (p. 1383) was acidified with excess of hydrochloric acid, when a thick, heavy oil separated, which on standing at the ordinary temperature for 3 weeks became much less dense and more mobile. The whole was then saturated with calcium chloride, repeatedly extracted with ether, the ethereal solution washed well with strong sodium carbonate (*d*), dried over calcium chloride, and evaporated. In this way, about 80 grams of an oil were obtained which distilled constantly at 163° (40 mm.), and had a rotation of $-4{\cdot}4°$ in a 100 mm. tube. This was further purified by solution in baryta water and treatment with hydrochloric acid at the ordinary temperature, as previously described in purifying the main bulk of the *cis*-lactones (p. 1382); it then yielded more than 70 grams of pure *cis*-lactones. Thus, without allowing for considerable loss during purification, the total yield of the *cis*-lactones from 250 grams of the mixed lactones

is at least 170 grams. The sodium carbonate extract *d* was treated in exactly the same way as *c*, and yielded small quantities of the *cis*-lactones and about 0·5 gram of pure crystalline A-acid.

The steam distillation flask, *a*, contained a considerable quantity of a thick oil; this was repeatedly extracted with ether and after drying the ethereal solution and evaporating, the residual oil was several times carefully distilled. During the first distillation, much water was given off and a colourless oil was collected at 160—170° under 35 mm. pressure, leaving in the flask a slight crystalline residue of camphoric anhydride which had escaped the action of the aluminium chloride. In order to remove this as far as possible, the oil was carefully dried and several times slowly fractionated under 35 mm. pressure, when almost the whole passed over at 155—160°.

When this oil was dissolved in baryta water and, after acidifying, the acids extracted with ether, an oil was obtained which, even after standing for months, deposited only a very few crystals; it was therefore distilled under the ordinary pressure, when almost the whole quantity came over at 252—255° (750 mm.) The distillate was dissolved in ether and repeatedly extracted with dilute potash, and the alkaline solution, after freeing from ether, was acidified, when a considerable quantity of an oil was precipitated which, on standing, became semi-solid.

In contact with a porous plate, the oily impurity was soon absorbed and a crystalline mass resulted, which after crystallising from dilute acetic acid melted at 78—80° and consisted of A-tetrahydro-xylic acid (p. 1392).

0·1481 gave 0·3802 CO_2 and 0·1224 H_2O. C = 70·0; H = 9·2.
$C_9H_{14}O_2$ requires C = 70·1; H = 9·1 per cent.

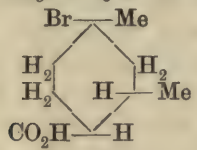
This acid, which weighed about 3 grams, is undoubtedly formed by the elimination of water from A-hydroxyhexahydro-xylic acid, during the frequent distillations, since it is elsewhere proved (p. 1391) that small quantities of A-tetrahydro-xylic acid are always produced when the A-hydroxy-acid is distilled. The ethereal solution which had been separated from the alkaline extract, gave, on evaporation, a colourless oil, and this was converted into the hydroxy-acid by treatment with baryta in the usual way.

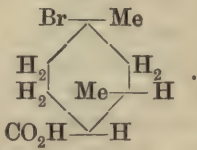
On long standing, the thick, oily acid partially crystallised and when spread on a porous plate a colourless mass of crystals was obtained, which, after recrystallisation from ether, melted at 158—160° and consisted of A-hydroxyhexahydro-xylic acid. The porous plate was broken up and extracted in a Soxhlet apparatus with ether, and the ethereal extract, after a long series of fractional crystallisations, yielded about 2 grams of A-hydroxy-acid and 5 grams of pure B-hydroxy-

hexahydro-xylic acid, which melted at 113° and on distillation was decomposed with elimination of water and formation of the pure B-lactone melting at 44°.

It is remarkable that so little of the B-acid should have been obtained on this occasion, because in the previous experiments (*loc. cit.*, p. 346), a relatively large quantity of it could always be isolated with comparative ease. This great difference in yield proves that the relative quantity of the lactones formed by the action of aluminium chloride on camphoric anhydride varies with unavoidable slight alterations in the conditions of the experiment.

Action of Hydrobromic Acid on the cis-*Lactones of Hydroxyhexahydro-xylic Acid. Formation of the* cis-*Modifications* (C and D) *of Bromohexahydro-xylic Acid,*





When the mixed *cis*-lactones, in quantities of not more than 5 grams are rapidly mixed with four times the volume of fuming hydrobromic acid (saturated at 0°), they rapidly and completely dissolve, but in a few seconds the solution becomes opaque owing to the separation of oil. The oil collects as a clear layer on the surface of the acid and after standing for 24 hours solidifies to a colourless, crystalline mass. This is powdered, washed with water on the pump, and left in contact with porous porcelain until quite dry; it is then ground up with light petroleum (b. p. 35—40°), in which it is very sparingly soluble, and washed with this solvent on the pump. The latter operation not only removes traces of coloured impurity but dissolves a small quantity of unchanged lactone, which always appears to be present, even when a large excess of hydrobromic acid is used. The colourless residue is *rapidly** dissolved in boiling light petroleum (b. p. 80—90°), a pinch of purified animal charcoal added, the liquid filtered, and carefully watched as it crystallises. A small crop of prismatic crystals of the C-bromo-acid quickly forms, then there is a pause in the crystallisation, and if the liquid is quickly poured off and well stirred, a mass of needles of the D-bromo-acid rapidly separates. By repeating this operation, it is quite easy to completely separate these two acids.

C-Bromohexahydro-xylic Acid crystallises in glistening, prismatic needles and melts at about 137—138° if the determination is rapidly

* Unless this operation is very rapidly performed, the bromo-acids decompose with evolution of quantities of hydrogen bromide.

carried out, but as it decomposes on heating with evolution of hydrogen bromide, a considerably lower melting point will be observed if th operation is conducted slowly. On analysis:

0·2108 gave 0·1697 AgBr. Br = 34·2

$C_9H_{15}O_2Br$ requires Br = 34·0 per cent.

This C-bromo-acid is very sparingly soluble in light petroleum and so similar in its other properties to A-bromohexahydro-xylic acid (m. p. 133°, p. 1391) that it was at first thought that the two were identical. Carefully purified specimens of each of these two acids were therefore intimately mixed, and it was then found that the melting point of the mixture was about 100—105°, a conclusive proof that the two bromo-acids C and A are not identical.

So far as could be seen with the small quantity of material at our disposal (2 grams dissolved in 100 c.c. of pure ether), C-bromohexahydro-xylic acid is inactive; in dissolves readily in sodium carbonate, and on acidifying the solution and heating to boiling, some of the tetrahydro-xylic acid formed appears to be converted into the C-lactone; if this is removed by making alkaline with sodium carbonate and extracting with ether and the alkaline solution acidified, an oil separates which solidifies on standing and probably consists of C-tetrahydro-xylic acid. From this small experiment, the C-bromo-acid appears to behave somewhat differently from the A-, B-, and D-bromo-acids, which do not yield lactones when treated in this way. This difference, however, requires confirmation before it can be definitely accepted.

The *D-bromohexahydro-xylic acid*, after complete separation from the C-acid by repeated recrystallisation from light petroleum, melts at about 128—130° and separates from light petroleum, in which it is sparingly soluble in the cold, as a voluminous mass of needles, which completely fill the liquid. It is readily soluble in ether and a solution in this solvent containing 5 grams in 100 c.c. was found, on examination, to be quite inactive.

It dissolves readily in dilute sodium carbonate, and on boiling the solution elimination of hydrogen bromide takes place with formation of *D-tetrahydro xylic acid* (see next section). An analysis of D-bromohexahydro-xylic acid yielded the following results:

0·1896 gave 0·1514 AgBr. Br = 34·1.

$C_9H_{15}O_2Br$ requires Br = 34·0 per cent.

It may, at first sight, seem remarkable that the bromo-acids C and D should show no signs of activity, although the *cis*-lactones from which they were prepared had a rotation of $-5·3°$ in a 100 mm. tube. It has, however, already been pointed out that, in the formation of these lactones from camphoric anhydride, racemisation must have taken

place, and the fact that the *cis*-lactones always have a small rotation simply shows that it has not been quite complete.

When the *cis*-lactones are converted into the bromo-acids and then purified by recrystallisation from light petroleum, the externally compensated modifications being less soluble (as is frequently the case) are easily obtained in a pure state, and the traces of the active modifications remain in the mother liquor.

That the light petroleum mother liquor of these inactive bromo-acids contains active substances was proved by direct experiment, but the solutions were unfortunately too highly coloured to allow of exact measurements being made.

D-Tetrahydro-xylic Acid, $C_8H_{15}\cdot CO_2H$.

D-Bromohexahydro-xylic acid dissolves readily in sodium carbonate solution, and if the solution is heated to boiling for a few seconds and then cooled and acidified, an acid separates either at once in the crystalline form, or else as an oil which rapidly solidifies. The solid mass, after drying on a porous plate, melts at about 80°, and is so soluble in organic solvents that it is difficult to purify it by recrystallisation.

It crystallises, however, in the form of pearly plates from dilute methyl alcohol, but the operation is rather troublesome, since, unless exactly the right conditions of concentration and temperature have been found, the acid always separates as an oil.

D-Tetrahydro-xylic acid melts at 87°, and distils without decomposition; it is almost insoluble in water, but readily volatile in a current of steam. On analysis:

0·1571 gave 0·4020 CO_2 and 0·1298 H_2O. C = 69·8; H = 9·2.

$C_9H_{14}O_2$ requires C = 70·1; H = 9·1 per cent.

When left in contact with fuming hydrobromic acid, this acid is rapidly converted into the D-bromohexahydro-xylic acid from which it had been prepared.

Oxidation of D-Tetrahydro-xylic Acid.—When this unsaturated acid is dissolved in dilute sodium carbonate and mixed with potassium permanganate, the latter is instantaneously reduced, and as it seemed probable that results throwing light on the position of the double linking in this acid (p. 1380) might be obtained by studying this oxidation, the following experiment was carried out.

The pure acid (5 grams) was dissolved in dilute sodium carbonate mixed with a quantity of powdered ice and oxidised, in a porcelain dish fitted with a turbine, with small quantities of permanganate until the colour remained permanent for 3 minutes. Sodium sulphite was then added to destroy the excess of permanganate, the

liquid heated to boiling, and the filtrate and washings of the manganese precipitate evaporated to a small bulk. The concentrated solution, after acidifying with acetic acid, gave no precipitate with calcium sulphate, showing that no oxalic acid had been formed. The whole was then acidified with hydrochloric acid and distilled in steam to remove a very small quantity of a volatile substance which appeared to be present. The residue in the steam distillation flask was saturated with ammonium sulphate, and repeatedly extracted with ether, the ethereal solution was dried over calcium chloride and evaporated, when a pale yellow oil was obtained which, after standing over sulphuric acid in a vacuum desiccator for some days, showed no signs of crystallising. It was analysed with the following result:

0·1571 gave 0·3290 CO_2 and 0·1105 H_2O. C = 57·1; H = 7·8.
$C_9H_{14}O_4$ requires C = 58·0; H = 7·5 per cent.

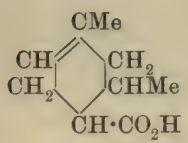
This acid is very readily soluble in water and is monobasic, since 0·207 gram was found, on titration with decinormal caustic soda, to neutralise 0·045 NaOH, whereas this amount of a monobasic acid, $C_9H_{14}O_4$ should have neutralised 0·044 NaOH.

The remainder of the acid was dissolved in water and oxidised with a slight excess of potassium dichromate and dilute sulphuric acid on the water-bath, the product was then saturated with ammonium sulphate and extracted 20 times with ether. After drying over calcium chloride and evaporating, an oil was obtained which on standing over sulphuric acid became semi-solid; when this was spread on a porous plate, the oily impurity was soon completely absorbed, leaving a hard, crystalline mass which melted roughly at 140°.

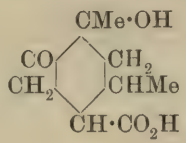
This crude acid is very soluble in water, but a concentrated solution on standing deposits colourless plates like sugar crystals which, after recrystallisation, melt at 167° with slight previous softening. On analysis:

0·1121 gave 0·2206 CO_2 and 0·0704 H_2O. C = 53·6; H = 7·0.
$C_9H_{14}O_5$ requires C = 53·5; H = 6·9 per cent.

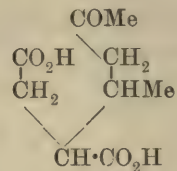
The new acid is dibasic, since 0·1076 gram required for neutralisation 0·0420 NaOH, whereas this quantity of a dibasic acid, $C_9H_{14}O_5$, should neutralise 0·0426 NaOH. It shows all the reactions of a ketonic acid, and when treated with potassium hydroxide and bromine it yields bromoform; it therefore probably contains the group Me·CO; unfortunately, the amount of material at our disposal was too small to allow of the isolation and identification of the acid which is formed during this oxidation. These results seem, nevertheless, to indicate the probability of the oxidation of D-tetrahydro-xylic acid proceeding somewhat in the following way



D-Tetrahydro-xylic acid.



Acid, $C_9H_{14}O_4$.



Acid, $C_9H_{14}O_5$ (m. p. 167°).

The position of the double-bond in D-tetrahydro-xylic acid has, of course, not been definitely ascertained, and the formula given here has simply been selected to serve as an illustration of the possible mechanism of the oxidation.

The Lactone of A-Hydroxyhexahydro-xylic Acid and its Conversion into A-Bromohexahydro-xylic Acid and into A-Tetrahydro-xylic Acid.

Twenty grams of pure A-hydroxyhexahydro-xylic acid (m. p. 160°) were distilled and the distillate dissolved in ether and extracted three times with carbonate of soda to remove traces of an acid which was present (see below). The ethereal solution was then dried over calcium chloride, evaporated and the residual lactone twice fractionated, when practically the whole quantity distilled at 263—265° under 748 mm. pressure the fraction boiling constantly at 264° being collected separately and forwarded to W. H. Perkin, sen., in order that its specific gravity and magnetic rotation might be determined. This specimen had a permanent rotation of +1·96° in a 100 mm. tube. The density and magnetic rotation determinations gave the following results:

Density. d 10°/10° = 1·0640; d 15°/15° = 1·0606; d 20°/20° = 1·0575.

Magnetic rotation.

t.	Sp. rotation.	Mol. rotation.
15·4°	1·0131	8·174.

This *trans*-lactone has therefore a higher sp. gr. and lower magnetic rotation than the *cis*-lactones (p. 1383). During its journey by train, it solidified to a hard mass of crystals which although very soluble in light petroleum (b. p. 30—35°), crystallised from this solvent in colourless needles melting at about 55°. On analysis:

0·1963 gave 0·5034 CO_2 and 0·1641 H_2O. C = 69·9; H = 9·2.
$C_9H_{14}O_2$ requires C = 70·1; H = 9·1 per cent.

In order to prove that this solid lactone was really the *lactone* of *A-hydroxyhydro-xylic acid*, it was warmed with a little baryta water,

in which it very readily dissolved with formation of the barium salt of the hydroxy-acid. The solution was acidified, extracted repeatedly with ether, and the ethereal solution, after drying over calcium chloride, evaporated to a small bulk, when crystalline crusts were deposited which melted at 160° and consisted of pure A-hydroxyhexahydro-xylic acid. The lactone of this acid was previously described (this vol., 345) as an oil boiling at 261—264° under 748 mm. pressure, and this specimen showed no signs of crystallising either after standing for 6 months or on cooling in a mixture of ice and salt ; when, however, a crystal of the lactone melting at 55° was put into the liquid, crystallisation started at once and the whole soon solidified to a hard mass of crystals.

The sodium carbonate solution which had been employed in purifying the lactone (see above) gave, on acidifying, no precipitate, but it was noticed that after standing for some days a small quantity of needle-shaped crystals had separated. These were collected and dried on a porous plate at the ordinary temperature ; they then melted at 80°, and were found to consist of pure A-tetrahydro-xylic acid (see below). It is therefore evident that A-hydroxyhexahydro-xylic acid on distillation is almost quantitatively converted into its lactone, but that a very small amount of the acid is decomposed in another direction with elimination of water and formation of A-tetrahydro-xylic acid.

A-Bromohexahydro-xylic Acid.—The lactone of A-hydroxyhexahydro-xylic acid dissolves rapidly and completely in fuming hydrobromic acid (saturated at 0°), but the solution soon becomes cloudy and an oily layer separates which becomes crystalline in a few minutes. After standing for about an hour, the hard, crystalline mass was ground up with water, washed well on the pump, dried on a porous plate at the ordinary temperature, and then rapidly recrystallised from boiling light petroleum (b. p. 60—70°). The minute, glistening prisms which rapidly separated were analysed, with the following results :

0·1511 gave 0·1121 AgBr. Br = 33·9.

$C_9H_{15}O_2Br$ requires Br = 34·0 per cent.

A-Bromohexahydro-xylic Acid melts at about 133° almost without decomposition ; it is readily soluble in most organic solvents, but only very sparingly so in cold light petroleum ; its solution in ether is inactive. In appearance and melting point it is so similar to C-bromohexahydro-xylic acid that we were at first inclined to believe in the identity of the two. We therefore mixed equal quantities of the pure substances, and found that the melting point of the mixture was about 100—105° ; it is therefore clear that the acids are not identical.

Considerable quantities of A-bromohexahydro-xylic acid were also prepared by grinding up A-hydroxyhexahydro-xylic acid with fuming

hydrobromic acid. The crystals of the acid become converted into a gummy mass, but this soon solidifies, and after washing well on the pump and drying on a plate, a mass of colourless crystals is obtained which consists of the almost pure A-bromo-acid.

A-Chlorohexahydro-xylic Acid. — When A-hydroxyhexahydro-xylic acid is boiled for a few seconds with concentrated hydrochloric acid, it does not yield the corresponding lactone, but is converted into an oil which, on cooling, solidifies. This was collected, washed well with water, and, after drying over sulphuric acid, rubbed on a porous plate with light petroleum (b. p. 35—40°) until free from traces of oil. The colourless, crystalline residue, which was not sufficient for recrystallisation, melted at about 92°, and, on analysis, gave numbers which showed that it evidently consisted of A-chlorohexahydro-xylic acid:

0·1547 gave 0·1146 AgCl. Cl = 18·3.

$C_9H_{15}O_2Cl$ requires Cl = 18·5 per cent.

A-Tetrahydro-xylic Acid.—This acid is readily obtained by dissolving A bromohexahydro-xylic acid in excess of sodium carbonate and boiling the solution for a few minutes; it separates on acidifying in an almost pure condition as a colourless, crystalline precipitate. For analysis, it was recrystallised from dilute acetic acid, and thus obtained in the form of colourless groups of needles, which melt at 80°:

0·1587 gave 0·4066 CO_2 and 0·1321 H_2O. C = 69·9; H = 9·2.

$C_9H_{14}O_2$ requires C = 70·1; H = 9·1 per cent.

The acid is almost insoluble in cold water; if, however, it is boiled with water, a small quantity dissolves, and on cooling separates in four-sided plates which melt at 80°; it is readily volatile in steam. Most organic solvents dissolve it freely, but it is comparatively sparingly soluble in cold light petroleum (b. p. 35—40°). The acid seems to have no tendency to yield a lactone on boiling with dilute acids; it separates, for example, unchanged from 20 per cent. sulphuric acid, even after boiling for 5 minutes. When mixed with fuming hydrobromic acid, it becomes soft, but does not dissolve, and from the mixture, after standing for 3 hours, water precipitates a mass of colourless crystals which, after washing with water, drying on a porous plate, and recrystallising from light petroleum, melts at 133°, and consists of pure A-bromohexahydro-xylic acid.

Oxidation of A-Tetrahydro-xylic Acid.—This acid, when dissolved in sodium carbonate, instantly decolorises permanganate, even at temperatures considerably below 0°, and it therefore seemed possible that, by studying this oxidation, results might be obtained which would throw some light on the position of the double bond in the molecule (see p. 1380).

Six grams of the pure acid were therefore dissolved in dilute sodium carbonate, mixed with powdered ice, and treated with a 3 per cent. solution of permanganate until the pink colour remained permanent for at least 2 minutes.

The slight excess was then removed with sodium sulphite, the whole heated to boiling, filtered, and the filtrate and washings of the manganese precipitate evaporated to a small bulk and tested for oxalic acid, but no trace of this acid could be detected. After acidifying and extracting repeatedly with pure ether, the ethereal solution was dried over calcium chloride and evaporated, when a thick, brownish, oily acid was obtained, which was left over sulphuric acid in a vacuum desiccator for 4 days and then analysed, with the following result:

0·1254 gave 0·2622 CO_2 and 0·0887 H_2O. C = 57·0; H = 7·9.
$C_9H_{14}O_4$ requires C = 58·0; H = 7·5 per cent.

This acid is readily soluble in water, and is evidently ketonic in character, since its aqueous solution gives at once a yellow, oily precipitate with phenylhydrazine acetate. That it is monobasic is shown by the results of the titration with decinormal sodium hydroxide, when 0·2366 gram required for neutralisation 0·0508 gram NaOH, whereas this quantity of a monobasic acid, $C_9H_{14}O_4$, should neutralise 0·0509 gram NaOH.

We next oxidised this acid with potassium dichromate and dilute sulphuric acid, exactly as described in the case of the isomeric acid from D-tetrahydro-xylic acid (p. 1389), and on extracting the product with ether, an oily acid was obtained which did not crystallise even after standing over sulphuric acid in a vacuum desiccator for some weeks. This oil gives an oily precipitate with phenylhydrazine acetate, and yields bromoform in considerable quantity when treated with bromine and potassium hydroxide; it is, therefore, evidently a ketonic acid, but as it did not solidify it was not further investigated.

Formation of B-Bromohexahydro-xylic Acid and of B-Tetrahydro-xylic Acid from the Lactone of B-Hydroxyhexahydro-xylic Acid.

The lactone used in these experiments was prepared by distilling the pure B-hydroxy-acid as described in the previous communication, it boiled at 258—260° under 745 mm. pressure and melted at 44°; it was particularly noticed that even after repeated distillation there was no appreciable alteration in the melting point, clearly proving that even at the high temperature of the distillation, no change into a *cis*-modification takes place. When this lactone is melted and mixed with three times its volume of fuming hydrobromic acid (saturated at 0°), it dissolves, but the solution suddenly becomes opaque and an oil

separates which begins to crystallise at once, the change from B-lactone to crystalline bromo-acid being apparently even more rapid than when the A-lactone is similarly treated (p. 1391). The product was mixed with water, the crystals collected, allowed to dry on a porous plate at the ordinary temperature, and then crystallised from light petroleum (b. p. 60—70°). On analysis:

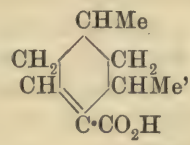
0·1520 gave 0·1212 AgBr. Br = 33·8.
$C_9H_{15}O_2Br$ requires Br = 34·0 per cent.

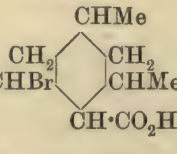
B-Bromohexahydro-xylic Acid melts at about 128° with decomposition, and is more readily soluble in light petroleum than the corresponding A-acid. It dissolves easily in sodium carbonate, and if the solution is boiled for a few minutes, then cooled and acidified, a crystalline precipitate separates which, after crystallising from dilute acetic acid, melts at about 68° and consists of B-tetrahydro-xylic acid.

0·1592 gave 0·4078 CO_2 and 0·1303 H_2O. C = 69·9; H = 9·1.
$C_9H_{14}O_2$ requires C = 70·1; H = 9·1 per cent.

B-Tetrahydro-xylic Acid is very sparingly soluble in cold water, but it may be crystallised from large quantities of boiling water; its solution in sodium carbonate instantly decolorises permanganate.

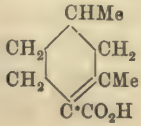
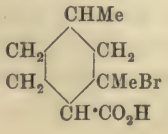
When left in contact with fuming hydrobromic acid, it becomes soft but does not dissolve, and if after 2 hours water is added, a white, crystalline precipitate separates which crystallises from light petroleum in woolly needles melting at 128° and consisting of pure B-bromohexahydro-xylic acid.

Δ^1-*Tetrahydro-xylic Acid*,  , *and its conversion into*

2-*Bromohexahydro-xylic Acid*,*  , *and into Xylic Acid.*

Δ^1-Tetrahydro-xylic acid is structurally isomeric with the tetrahydro-xylic acids, A, B, and D, and is the acid which is formed when

* The only other formulæ possible for these acids are:

 and 

xylic acid is reduced with sodium and *iso*amyl alcohol, and when methyl α-bromohexahydro-xylate is hydrolysed with alcoholic potash (Bentley and Perkin, Trans., 1897, 71, 173; Lees and Perkin, this vol., 338), it melts at 107°. When it is mixed with fuming hydrobromic acid, it does not readily dissolve, but the crystals are seen to undergo gradually a change in appearance. In order to ensure the reaction being complete, the mixture was sealed up in a tube and shaken from time to time, and after two days water was added, the crystals collected on the pump, and allowed to dry on a porous plate in contact with air. The substance then melted at about 124—125°, but after crystallising from light petroleum (b. p. 50—60°), colourless, glistening prisms were obtained which melted at 127° without decomposition. On analysis:

0·152 gave 0·1208 AgBr. Br = 33·8.

$C_9H_{15}O_2Br$ requires Br = 34·0 per cent.

When treated with sodium carbonate, *2-bromohexahydro-xylic acid* shows quite a different behaviour from that observed in the case of the A, B, and D-bromohexahydro-xylic acids (pp. 1388, 1392, 1394). It dissolves at first in the sodium carbonate, forming a clear solution which then rapidly becomes cloudy, and an oil separates which is very readily volatile in steam, smells like a hydrocarbon, and is evidently tetrahydro-*m*-xylene.

$$C_9H_{15}O_2Br = C_8H_{14} + HBr + CO_2.$$

After boiling until the hydrocarbon was expelled, the clear solution gave on acidifying a colourless, crystalline precipitate which, when drained on a tile and dried at 90°, melted sharply at 107—108°, and evidently consisted of Δ^1-tetrahydro-xylic acid.

Action of Sulphuric Acid on Δ^1*-Tetrahydro-xylic Acid.*—This acid dissolves in concentrated sulphuric acid, and when the solution is heated at 100° for 10 minutes, sulphur dioxide is rapidly evolved and the dark coloured liquid, on dilution with water, deposits a yellow, crystalline precipitate. This was collected, distilled, and recrystallised from dilute acetic acid, when colourless crystals were obtained which melted at 124° and consisted of xylic acid. It is therefore evident that, in its behaviour with hydrobromic acid and with sulphuric acid Δ^1-tetrahydro-xylic acid shows the greatest similarity to the A, B, and D tetrahydro-xylic acids described in this paper.

In conclusion we wish to express our thanks to Professors F. S. Kipping and W. J. Pope for many valuable suggestions that they were good enough to make during the course of this research.

We also wish to state that the cost of the large amount of material which was required in this research has been to a large extent defrayed by repeated grants from the Government Grant Fund of the Royal Society.

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CIS- AND TRANS-TETRAMETHYLENE-(1 : 3)-DICARBOXYLIC ACIDS AND THE CONDENSATION OF FORMALDEHYDE WITH ETHYLIC MALONATE.

BY

E. HAWORTH

AND

W. H. PERKIN, JUNR.

From the Transactions of the Chemical Society, 1893.

Cis- and *trans*-Tetramethylene-(1 : 3)-dicarboxylic Acids and the Condensation of Formaldehyde with Ethylic Malonate.

By E. Haworth and W. H. Perkin, junr.

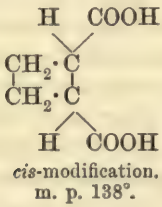
In a communication made to this Society some time since by one of us (Trans., 1890, **57**, 18), it was shown that the disodium compound of ethylic butanetetracarboxylate is readily acted on by bromine with the formation of ethylic tetramethylenetetracarboxylate,

$$\begin{matrix}CH_2\cdot CNa(COOC_2H_5)_2\\ CH_2\cdot CNa(COOC_2H_5)_2\end{matrix} + Br_2 = \begin{matrix}CH_2\cdot C(COOC_2H_5)_2\\ CH_2\cdot C(COOC_2H_5)_2\end{matrix} + 2NaBr.$$

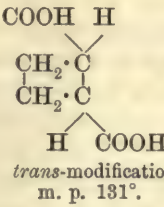
From this ethereal salt, by hydrolysis and elimination of two mols. of CO_2 at 200°, the anhydride of tetramethylene-1 : 2-dicarboxylic acid is formed thus.

$$\begin{matrix}CH_2\cdot C(COOH)_2\\ CH_2\cdot C(COOH)_2\end{matrix} = \begin{matrix}CH_2\cdot CH\cdot CO\\ CH_2\cdot CH\cdot CO\end{matrix}\!\!>\!O + 2CO_2 + H_2O.$$

A subsequent very careful examination of this synthesis (Trans., 1894, **65**, 572) enabled us to show that the tetramethylenedicarboxylic acid (1 : 2) formed in this way was, like hexahydrophthalic acid, capable of existing in well-defined *cis-* and *trans*-modifications, which may be represented by the formulæ,



cis-modification.
m. p. 138°.



trans-modification.
m. p. 131°.

The *cis*-acid readily yields an anhydride (melting at 32°), but it was not found possible to prepare an anhydride of the *trans*-acid; if however, the *trans*-acid is distilled, it yields the anhydride of the *cis*-acid, and, *vice versa*, the *cis*-acid is completely converted into the *trans*-acid by heating with hydrochloric acid at 180°. It is evident from this method of formation that these acids are tetramethylenedicarboxylic acids, and their properties clearly prove that their isomerism is due to stereochemical grounds, and not to a difference in chemical structure.

Tetramethylene-1 : 3-*dicarboxylic acid*, $COOH\cdot CH\!<\!\begin{matrix}CH_2\\ CH_2\end{matrix}\!>\!CH\cdot COOH$,

isomeric with the above acids, was first obtained by Markownikoff and Krestownikoff (*Annalen*, 1881, **208**, 333) by the hydrolysis of the ethereal salt which is formed when ethylic α-chloropropionate is heated with dry sodium ethoxide.

$$\begin{matrix} COOC_2H_5\cdot CHCl\cdot CH_3 \\ CH_3\cdot CHCl\cdot COOC_2H_5 \end{matrix} = \begin{matrix} COOC_2H_5\cdot CH\text{—}CH_2 \\ CH_2\text{—}CH\cdot COOC_2H_5 \end{matrix} + 2HCl$$

This beautifully crystalline substance, which was called paratetrylenedicarboxylic acid, melts at 170—171°, and yields a double anhydride, $C_4H_6(CO\cdot C_2H_3O)_2$, when its silver salt is treated with acetyl chloride.

When this anhydride is distilled, it undergoes an interesting change, and the distillate is found to consist of a new anhydride, $C_4H_6\begin{matrix} CO \\ CO \end{matrix}O$, which, when pure, melts at 49—50°, and on treatment with water yields a dibasic acid, $C_4H_6(COOH)_2$, melting at 138°.

Markownikoff supposes that these changes take place in the following way.

$$\begin{matrix} CH_2\cdot CH\cdot COOAc \\ COOAc\cdot CH\cdot CH_2 \end{matrix} \rightarrow \begin{matrix} CH_2\cdot CH\cdot CO \\ CH_2\cdot CH\cdot CO \end{matrix}O \rightarrow \begin{matrix} CH_2\cdot CH\cdot COOH \\ CH_2\cdot CH\cdot COOH \end{matrix}$$

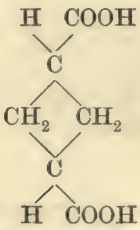
Anhydride, m. p. 49—50°. Acid, m. p. 138°.

That is to say, he assumes that the tetramethylene-1 : 3-dicarboxylic acid, which is a derivative of glutaric acid, has during this process undergone molecular change, and become converted into 1 : 2-tetramethylenedicarboxylic acid, called by him orthotetrylenedicarboxylic acid, which is a derivative of succinic acid. It is extremely improbable that such simple reactions would bring about such a fundamental change of composition, and Markownikoff's interpretation is clearly shown to be incorrect when the substances which he assumes to have the formulæ $\begin{matrix} CH_2\cdot CH\cdot CO \\ CH_2\cdot CH\cdot CO \end{matrix}O$ and $\begin{matrix} CH_2\cdot CH\cdot COOH \\ CH_2\cdot CH\cdot COOH \end{matrix}$ are directly compared with the compounds having these constitutions which were obtained by us in the way described at the commencement of this paper. Thus, for example, although both the acids melt at 138°, the anhydride of *cis*-tetramethylene-1 : 2-dicarboxylic acid melts at 32°, whereas the melting point of the anhydride of Markownikoff's acid is 49—50°, and there are many other ways in which the acids differ, as will be shown in detail in this paper.

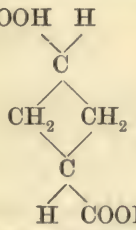
In Beilstein's *Handbuch* (vol. I., pp. 717—718) both *cis*-tetramethylene-1 : 2-dicarboxylic acid and Markownikoff's acid melting at 138° are represented as having the same formula, in spite of their being different substances, and as this has caused considerable confusion in the chemistry of the tetramethylene compounds, we decided to

investigate Markownikoff's acid with a view of determining its nature.

If we examine the formula of tetramethylene-1 : 3-dicarboxylic acid, it is at once apparent that this acid, like the corresponding (1 : 2) acid, should be capable of existing in the following two stereoisomeric forms.



cis-modification.



trans-modification.

and by repeating Markownikoff's work and also by means of new data, we have, as we think, been able to show conclusively that the isomerism of the ortho- and para-tetrylenedicarboxylic acids is simply due to the fact that they are the *cis*- and *trans*-modifications of 1 : 3-tetramethylenedicarboxylic acid. We found, in the first place, that the ethereal salt formed by the action of sodium ethoxide on ethylic chloropropionate, on hydrolysis, gives not only paratetrylenedicarboxylic acid melting at 171°, but also an acid melting at 133—135°, which, on examination, proved to be identical with orthotetrylenedicarboxylic acid, and the presence of which, in the product of hydrolysis, seems to have been overlooked by Markownikoff. This is strong evidence in favour of the acids being stereoisomeric, as it is quite usual to find the *cis*- and *trans*-forms produced together in such synthetical experiments as those described above. Then, again, the properties of the two acids are such as are commonly shown by stereoisomeric substances. Thus, para-tetrylenedicarboxylic acid, like *trans*-1 : 2-tetramethylenedicarboxylic acid, does not yield an anhydride, but on distillation it yields the anhydride of orthotetrylenedicarboxylic acid, just as *trans*-1 : 2-tetramethylenedicarboxylic acid, on distillation, is converted into the anhydride of the *cis*-acid. The reverse change, that is, the conversion of ortho- into para-tetrylene acid by heating with hydrochloric acid at 180°, we have, so far, not been able to accomplish, since, under these conditions, further decomposition of the product evidently occurs with formation of syrupy acids which we have not further investigated.

During the course of this research, we were led to again investigate the condensation of formaldehyde with ethylic malonate, in the hope that in this way a method might be devised by which the tetrylenic acids could be obtained with much less labour and in much better yield

than is the case when Markownikoff's method is employed. It was conceivable that 2 mols. of formaldehyde might readily condense with 2 mols. of ethylic malonate according to the scheme

$$(COOC_2H_5)_2CH_2 \begin{matrix} CH_2O \\ CH_2O \end{matrix} CH_2(COOC_2H_5)_2 =$$

$$(COOC_2H_5)_2C<\begin{matrix} CH_2 \\ CH_2 \end{matrix}>C(COOC_2H_5)_2$$

yielding ethylic tetramethylene-1 : 1 : 3 : 3-tetracarboxylate. From this ethereal salt, by hydrolysis and elimination of 2 mols. CO_2, the tetrylenic acids would be produced thus

$$(COOH)_2C<\begin{matrix} CH_2 \\ CH_2 \end{matrix}>C(COOH)_2 = COOH\cdot CH<\begin{matrix} CH_2 \\ CH_2 \end{matrix}>CH\cdot COOH + 2CO_2,$$

and, as will be shown later, it was actually found that the action does to some extent proceed in this way, but unfortunately the yield of tetrylenic acid, thus obtained, is only very small.

The condensation of ethylic malonate with formaldehyde was first investigated by one of us in 1886 (Perkin, *Ber.*, **19**, 1053), acetic anhydride being employed as the dehydrating agent, and it was then shown that the principal product of the reaction was *ethylic propanetetracarboxylate*,

$$2(COOC_2H_5)_2CH_2 + CH_2O = (COOC_2H_5)_2CH\cdot CH_2\cdot CH(COOC_2H_5)_2 + H_2O.$$

It was, however, mentioned that a small quantity of an oil, boiling at 208—212°, was also isolated, which on analysis gave numbers agreeing with those required by *ethylic methylenemalonate*, a substance which might easily have resulted from the condensation of 1 mol. of ethylic malonate with 1 mol. of formaldehyde according to the equation

$$CH_2O + CH_2(COOC_2H_5)_2 = CH_2{:}C(COOC_2H_5)_2 + H_2O.$$

In 1894 (*Ber.*, **27**, 2345), Knoevenagel published the results of an investigation on the condensation of ethylic malonate with formaldehyde in the presence of diethylamine as the condensing agent; in this way he obtained a good yield of ethylic propanetetracarboxylate which he converted into glutaric acid by hydrolysis and elimination of 2 mols. CO_2. Knoevenagel makes no mention of any previous paper on the subject, and appears to be ignorant of the fact that practically the whole of his results, including the preparation of glutaric acid, had been described in detail eight years previously (Perkin, *loc. cit.*).

In a long course of experiments which we have made in connection with this research on the condensation of formaldehyde with ethylic malonate, we have usually employed diethylamine instead of acetic

anhydride as the condensing agent, as it is more convenient and appears to lead to the same products. We find that, under the conditions described in this paper, the product of the reaction is a complicated mixture containing

Ethylic methylenemalonate, $(COOC_2H_5)_2C{:}CH_2$,

Ethylic propanetetracarboxylate,

$$(COOC_2H_5)_2CH{\cdot}CH_2{\cdot}CH(COOC_2H_5)_2,$$

Ethylic tetramethylenetetracarboxylate,

$$(COOC_2H_5)_2C<\begin{matrix}CH_2\\CH_2\end{matrix}>C(COOC_2H_5)_2.$$

and other substances of higher boiling point which are at present under investigation.

Ethylic methylenemalonate was isolated from the product of the reaction in the form of a polymeride which resembles white wax in appearance, and melts at about 150° ; this modification we have named ethylic paramethylenemalonate.

This remarkable substance, on distillation, is decomposed into an oil boiling constantly at 208—210°, and into very interesting higher boiling products which are at present under investigation. The numbers obtained in the analysis of the oil boiling at 208—210° agree exactly with those required for ethylic methylenemalonate, $(COOC_2H_5)_2C{:}CH_2$, and the fact that it boils only a few degrees higher than ethylic malonate (b. p. 198°), proves that it must have this simple composition. If the oil, directly after distillation, is dissolved in chloroform and the well-cooled solution treated with bromine, the halogen is instantaneously absorbed with formation of ethylic $\alpha\beta$-dibromethane-$\alpha\alpha$-dicarboxylate, $(COOC_2H_5)_2CBr{\cdot}CH_2Br$.

If, however, the fraction 208—210° is allowed to stand for 24 hours, at first sight no change appears to have taken place, but on closer examination it is seen that the oil has become converted into a hard and perfectly transparent polymeride, which melts, although not sharply, at a very high temperature and is quite different from the para-polymeride; this modification we have named ethylic meta-methylenemalonate.*

We have no doubt that the substance boiling at 208—212°, which was described and analysed in the first research on this subject (*loc. cit.*, p. 1054), was ethylic methylenemalonate. The fact that it polymerised on standing in the way it does was at the time overlooked.

Ethylic paramethylenemalonate behaves in a remarkable way when

* For want of a better system of nomenclature, we have used the prefixes *para* and *meta* here in the same sense as they are used in paraldehyde and metaldehyde, and it appears to us that in doing so there is very little danger of these names being confused with para- and meta-compounds in the aromatic series.

hydrolysed with alcoholic potash, as under these conditions it yields *cis*-tetramethylene-1 : 3-dicarboxylic acid, but it is nevertheless not the ethereal salt of this acid, since this substance, which we obtained in quantity by the action of sodium ethoxide on ethylic chloropropionate, is a colourless oil which distils without decomposition and shows no signs of polymerising. During the course of our experiments on the polymeric forms of ethylic methylenemalonate, many attempts were made to determine the molecular weights of these polymerides by means of the cryoscopic method, using acetic acid as a solvent; but the results obtained were most unsatisfactory, and the same want of success attended all our attempts to determine the vapour density of the polymerides in a vacuum.

The ethylic paramethylenemalonate described in this paper is probably identical with a polymeric form of ethylic methylenemalonate, which Zelinsky (*Ber.*, 1889, **22**, 3294) obtained by the action of methylene iodide on the sodium derivative of ethylic malonate, and which he describes as having properties like paraffin wax and melting at 155—156°. The molecular weight of this substance, which Zelinsky determined in acetic acid solution by the cryoscopic method, gave results agreeing closely with those required by the formula $[(COOC_2H_5)_2C{:}CH_2]_2$, and this chemist noticed that the polymeride, on distillation, yielded an oil boiling between 120° and 210°, from which, by the action of bromine, he obtained a dibromide boiling at 185—190° (75—85 mm.), and having approximately the composition $C_8H_{12}Br_2O_4$, that is, that of ethylic dibromethanedicarboxylate.

When the product of the condensation of formaldehyde with ethylic malonate is distilled under reduced pressure, an oil is obtained boiling at 250—300° (40 mm.); that this oil contains ethylic 1 : 1 : 3 : 3-tetramethylenetetracarboxylate appears to us to be proved by the fact that, in hydrolysis, it yields an oily acid, from which, by treatment in the manner described in detail in the experimental part of this paper, *cis*-1 : 3-tetramethylenedicarboxylic acid was isolated in quantity sufficient for analysis and identification.

Besides ethylic tetramethylenetetracarboxylate, there are other substances of interest produced during the condensation of formaldehyde with ethylic malonate; these are at present under examination, and we are also engaged in an investigation of the products formed when methylene iodide acts on the disodium compound of ethylic propanetetracarboxylate.

Action of Sodium Ethylate on Ethylic α-Chloropropionate. Formation of Cis- *and* Trans-*Tetramethylene*-1 : 3-*dicarboxylic Acids.*

In our first experiments on this reaction, we followed closely the method given by Markownikoff (*Annalen*, 1881, **208**, 334); subsequently, however, we introduced some modifications of importance, which enabled us to prove that the product of the reaction contained the ethylic salts of both the *cis*- and *trans*-tetramethylenedicarboxylic acids, and not only that of the latter, as Markownikoff seems to indicate.

Ethylic α-chloropropionate (45 grams) was heated in an oil bath to about 60—70° in a flask which was connected by means of a cork and bent tube to a small condenser; and dry* sodium ethoxide (containing 7·5 grams of sodium) was added in small quantities at a time, a stream of dry hydrogen being passed continuously through the apparatus during the operation. As each small quantity of sodium ethoxide was added, a vigorous action took place, the temperature rising to the point of ebullition, but the process was carefully regulated so that only traces of ethylic chloropropionate distilled over. During the progress of the decomposition, it was found advantageous to raise the temperature of the oil bath once or twice to 100° for a short time, in order to drive off as much as possible of the alcohol which had been formed during the reaction.

After all the sodium ethylate had been added, the temperature was kept at 100° for about half an hour; the mixture was then cooled, decomposed by dilute sulphuric acid, and the oily products extracted with ether. The ethereal solution, washed with sodium carbonate solution and with water, was dried over calcium chloride and evaporated, and the dark brown, oily residue distilled under the ordinary pressure until the temperature rose to 200°. The residue was then distilled under reduced pressure, and after two fractionations a good deal of oil was obtained boiling between 173° and 178° (110 mm.).

The yield of this oil, which on examination was found to consist of the mixed ethylic salts of *cis*- and *trans*-tetramethylenedicarboxylic acids, was only 10 per cent. of the ethylic chloropropionate employed, and this led us to make experiments on the action of sodium ethoxide on ethylic α-bromopropionate, as it seemed likely that the decomposition would take place more readily in this case. The results of these experiments showed, however, that although the reaction proceeded in the same way, the yield of ethylic tetramethylenedicarboxylate was even less than in the case of the ethylic chloro-

* This was freed as far as possible from alcohol by heating at 200° in a stream of dry hydrogen.

propionate, the actual amount obtained being never more than 5 per cent. of the ethylic bromopropionate employed.

The crude ethylic tetramethylenedicarboxylate, boiling at 173—178° (110 mm.), was dissolved in methylic alcohol and hydrolysed by boiling with potash in a reflux apparatus for 2 hours; the dark-coloured product was then mixed with water, and the solution evaporated on the water bath, with the frequent addition of small quantities of water, until every trace of methylic alcohol had been removed.

The concentrated solution, acidified with hydrochloric acid, was extracted many times with pure ether; and the ethereal solution of the mixed acids, after being dried over calcium chloride, was filtered and evaporated, and the oily residue placed over sulphuric acid in a vacuum desiccator. As this residue, even on long standing, only partially crystallised, it was dissolved in a little water and the solution saturated with hydrogen chloride, when crystals gradually separated. These were collected, washed with hydrochloric acid, and dried at 100°; they then melted at 166—169°, but on subsequently recrystallising from hydrochloric acid, the melting point rose to 170—171°. This beautiful, colourless, crystalline acid gave the following results on analysis.

0·1490 gave 0·2720 CO_2 and 0·0736 H_2O. C = 49·79; H = 5·49.
$C_4H_6(COOH)_2$ requires C = 50·00; H = 5·55 per cent.

This acid is trans-*tetramethylene*-1 : 3-*dicarboxylic acid*, identical with the acid of the same melting point obtained by Markownikoff, and called by him paratetrylenedicarboxylic acid or homoitaconic acid.

Cis-tetramethylenedicarboxylic acid, $COOH\cdot CH<\begin{matrix}CH_2\\CH_2\end{matrix}>CH\cdot COOH$.

So far as we have been able to discover, Markownikoff did not examine the mother liquors from the crystallisation of *trans*-tetramethylenedicarboxylic acid (see previous section); as, however, it seemed probable that these might contain the *cis*-acid, we subjected them to careful investigation. The combined hydrochloric acid liquors from a long series of experiments were filtered, evaporated to a small bulk on the water bath, and the residue placed over solid potash in a vacuum; after some time, crystals began to form, and during some months these gradually increased until the whole had assumed a pasty consistency. The mass, spread on porous porcelain, was left for some weeks until the mother liquor had been entirely absorbed, and the crystals were then dissolved in water, the solution boiled with pure animal charcoal, filtered, and saturated with gaseous hydrogen chloride. As the solution did not deposit crystals on standing, it was

placed over solid potash in a vacuum desiccator and allowed to concentrate gradually when after some days crystals separated, which were collected and drained on porous porcelain. As these crystals, dried at 100°, melted not very sharply at 128—133°, they were recrystallised, the operation being carried out exactly as before, except that the first few crystals, which it was thought might contain traces of the *trans*-acid, were neglected.

In this way, colourless crystals were obtained which melted at 129—133°, and on analysis gave the following numbers.

0·1380 gave 0·2497 CO_2 and 0·0704 H_2O. C = 49·34 ; H = 5·67.
$C_4H_6(COOH)_2$ requires C = 50·0 ; H = 5·55 per cent.

Although the melting point of this acid was somewhat low, the examination of its properties clearly indicated that it was *cis*-tetramethylenedicarboxylic acid, which, according to Markownikoff, when perfectly pure melts at 138—139°. In order to be quite sure of this identity, the acid was digested for half an hour with excess of acetyl chloride, and the solution allowed to evaporate slowly over potash ; the mass of beautiful, needle-shaped crystals thus obtained, after being drained on a plate, melted at 50—51°, and consisted of pure *cis*-tetramethylenedicarboxylic anhydride.

0·1210 gave 0·2529 CO_2 and 0·0534 H_2O. C = 57·01 ; H = 4·90.
$C_4H_6(C_2O_3)$ requires C = 57·14 ; H = 4·76 per cent.

This anhydride was reconverted into the acid, which then melted at 135—136°.

Action of Acetic Anhydride on trans-*Tetramethylene*-1 : 3-*dicarboxylic Acid.*

Two experiments on the action of acetic anhydride on *trans*-tetramethylene-1 : 3-dicarboxylic acid were made, with the following results.

(1) Two grams of the pure acid were warmed with a large excess of etic anhydride until it just dissolved. The solution was then placed a desiccator containing caustic potash and allowed to evaporate in vacuum.

(2) A similar solution of the acid in acetic anhydride was boiled in reflux apparatus for 6 hours, and the solution then evaporated over caustic potash in a vacuum.

The product of both experiments was a thick syrup, which only showed signs of crystallising after being kept for several weeks. Both products had the same composition, and consisted of a double anhydride of acetic and *trans*-tetramethylenedicarboxylic acids, as is shown by the following analyses and experiments.

(1) 0·1456 gave 0·0697 H_2O and 0·2807 CO_2. C = 52·58; H = 5·32.
(2) 0·1500 „ 0·0730 H_2O „ 0·2895 CO_2. C = 52·64; H = 5·40.
$C_4H_6(CO_2 \cdot C_2H_3O)_2$ requires C = 52·63; H = 5·26 per cent.

Both products dissolved in boiling water, and on cooling the solutions, crystals of *trans*-tetramethylenedicarboxylic acid melting between 170° and 171° were deposited. The presence of the acetyl groups was proved in the following manner. The syrup was warmed with a solution of sodium carbonate, and the liquid, after being acidified with dilute sulphuric acid, was submitted to steam distillation until the distillate was no longer acid. The distillate, when neutralised with barium carbonate, gave a red coloration with ferric chloride, changing to a brown precipitate on boiling. The solution of the barium salt was concentrated, and the sparingly soluble silver salt obtained from it was analysed, when it gave numbers corresponding with those required for silver acetate, $CH_3 \cdot COOAg$.

Found C = 14·19; H = 1·97; Ag 64·59.
Theory C = 14·37; H = 1·79; Ag 64·66 per cent.

The results of these experiments confirm Markownikoff's statement that *trans*-tetramethylenedicarboxylic acid (paratetrylenedicarboxylic acid) is converted into a double anhydride, $C_4H_6(CO_2C_2H_3O)_2$, when its silver salt is treated with acetyl chloride.

Condensation of Formaldehyde with Ethylic Malonate.

As was mentioned in the introduction, the condensation of formaldehyde with ethylic malonate was first investigated by one of us in 1886 (*Ber.*, 19, 1053), with the result that, besides ethylic propanetetracarboxylate, $(COOC_2H_5)_2 \cdot CH \cdot CH_2 \cdot CH(COOC_2H_5)_2$, a small quantity of an oil was obtained which boiled at 208—212°, and on analysis gave numbers agreeing with the formula of ethylic methylenemalonate, $CH_2{:}C(COOC_2H_5)_2$. It was stated at the time that the experiments were to be continued, and as we required ethylic propanetetracarboxylate for our synthetical work in the course of this research, we used the opportunity for investigating the condensation of formaldehyde and ethylic malonate in more detail than had previously been done.

In the first experiments, acetic anhydride was used as the condensing agent, but on this occasion we have usually employed diethylamine, as we found that this base, which has been recommended by Knoevenagel (*Ber.*, 1894, 27, 2345) for this purpose, is more convenient in working with large quantities.

Ethylic malonate (160 grams) is mixed with a 40 per cent. solution of formaldehyde (60 grams) and alcohol added until the solution becomes clear; the mixture is allowed to stand at the ordinary tempera-

ture for 12 hours, and then heated on the water bath for 2 hours in a reflux apparatus. After cooling, about three times the volume of ether is added, the ethereal solution washed first with a solution of sodium carbonate, then with water, dried over calcium chloride, the ether evaporated, and the residual oil repeatedly fractionated under reduced pressure, the fractions collected being the following.

I. 130—190° (70 mm.). II. 210—230° (40 mm.).
III. 250—300° (40 mm.).

These were then further investigated as described in the following sections.

Ethylic Methylenemalonate, $CH_2{:}C(COOC_2H_5)_2$.

The oil obtained by the condensation of formaldehyde with ethylic malonate as described in the previous section, and boiling at 130—190° (70 mm.), was distilled under the ordinary pressure, when it showed the following behaviour. The liquid began to boil at 190°, and a small quantity of oil, consisting possibly of unchanged ethylic malonate, passed over between this and 200°; the temperature then rose rapidly to 205°, about half the oil distilling between this and 215°. As the remainder of the oil proved to have a very high boiling point, the distillation was continued under reduced pressure, and in this way large fractions were obtained boiling at 210—230° and 250—300° under a pressure of 40 mm.; these were added to the similar fractions obtained as described in the previous section. This behaviour appears to indicate that during distillation under the ordinary pressure condensation must take place between some of the constituents of the oil, and this was subsequently proved to be the case.

On standing for some days, the fraction boiling at 200—212°, under ordinary pressure, solidified almost completely to a hard, wax-like mass; this was ground up, left in contact with porous porcelain for some days, and then washed with light petroleum, in which it is insoluble, in order to remove any traces of oily impurity. The residue, which in appearance closely resembles paraffin wax, gave on analysis the following results.

0·1218 gave 0·2460 CO_2 and 0·0786 H_2O. C = 55·08; H = 7·17.
0·1620 „ 0·3318 CO_2 „ 0·1000 H_2O. C = 55·80; H = 6·86.
0·1456 „ 0·2980 CO_2 „ 0·0917 H_2O. C = 55·82; H = 7·01.
$CH_2{:}C(COOC_2H_5)_2$ requires C = 55·81; H = 6·98 per cent.

This substance, which we propose to call *para*-ethylic methylenemalonate, is a polymeric form of ethylic methylenemalonate and evidently identical with the substance which Zelinsky (*Ber.*, 1889, **22**, 3294) obtained by the action of methylene iodide on the sodium derivative of ethylic malonate.

When heated in a capillary tube, it begins to melt at about 146° and is completely melted at 150°, whilst at a somewhat higher temperature gas begins to be evolved, the decomposition being rapid at 200°. The polymeride is very sparingly soluble in alcohol, ether, light petroleum, and benzene, but dissolves moderately readily in warm acetic acid, and owing to this we made several attempts to determine its molecular weight by Raoult's method, but the results were very unsatisfactory, as, although in two experiments values were obtained which seemed to indicate that the substance had the formula $2CH_2{:}C(COOC_2H_5)_2$, the results were not constant, much higher values being obtained in some experiments than in others.

The polymeride of ethylic methylenemalonate prepared by Zelinsky, melted at 155—156° and had properties similar to those of the substance described above; in one experiment, using acetic acid as the solvent, Zelinsky obtained numbers for the depression of the freezing point which led him to conclude that the polymeride had the formula $2CH_2{:}C(COOC_2H_5)_2$, but when the insolubility of the substance and its general properties are taken into account it appears to us that it must have a very much higher molecular weight.

Distillation of Para-Ethylic Methylenemalonate. Formation of Ethylic Methylenemalonate and its Meta-Polymeride.

When heated cautiously in a small distillation flask with a naked flame, para-ethylic methylenemalonate first melts and then decomposes with effervescence and evolution of a vapour possessing a very pungent and penetrating smell, something like that of formaldehyde. On heating more strongly, distillation soon commences and nearly the whole passes over between 205° and 250° as a pale yellow oil, but a small quantity of an oil of higher boiling point and some carbonaceous matter remains in the distillation flask.

On refractioning the distillate, about one-fourth distilled between 205° and 215°, and from this, on again fractioning, a considerable quantity of a colourless, pungent oil passed over constantly at 208—210°.* This, on analysis, gave the following numbers.

0·1601 gave 0·3268 CO_2 and 0·1010 H_2O. C = 55·70; H = 7·01.

$CH_2{:}C(COOC_2H_5)_2$ requires C = 55·81; H = 6·98 per cent.

As this oil boils at a temperature only slightly higher than ethylic malonate (b. p. 198°), it is clear that it consists of ethylic methylenemalonate and is not a polymeride; this view is borne out by the

* This oil is obviously identical with the substance (b. p. 208—212°) previously isolated by one of us (*Ber.*, 1886, **19**, 1053) from the products of the condensation of ethylic malonate with formaldehyde in the presence of acetic anhydride; the analysis of this oil gave C = 55·40; H = 7·31 per cent.

general properties of the substance. It is readily soluble in the usual organic solvents and its solution in chloroform decolorises bromine without the evolution of hydrogen bromide. In order to investigate this action, about 1 gram of the pure substances was, directly after distillation, dissolved in chloroform, cooled well, and a solution of bromine in chloroform run in until the colour just remained permanent. The chloroform was then removed by passing a current of dry air, and the residual oil analysed with the following result.

0·2120 gave 0·2450 AgBr. Br = 49·19.

$C_8H_{12}Br_2O_4$ requires Br = 48·19 per cent.

These numbers agree sufficiently well to show that the ethylic methylenemalonate has, during this reaction, united with 2 atoms of bromine with formation of *ethylic αβ-dibromoethane-αα-dicarboxylate*, and it is our intention to prepare this compound in larger quantities in order to examine its properties in detail.

When ethylic methylenemalonate boiling at 208—210° is kept, it rapidly polymerises, undergoing hardly any change in appearance, and in 24 hours it is completely converted into a hard, perfectly transparent polymeride, which is quite different in properties from the opaque, waxy-like *para*-ethylic methylenemalonate : for this new polymeride we propose the name *meta-ethylic methylenemalonate*.

This polymeride is very like horn in consistency, being very difficult to break, although it can be cut into shavings with a knife ; it is very sparingly soluble in the usual solvents, and when heated in a capillary tube it sinters at about 225°, and between 240° and 250° the soft mass gives off gas and decomposes without any definite melting point being observable.

When a small piece is heated in a test tube, it becomes soft and gives off a pungent gas smelling like formaldehyde, the soft mass then suddenly melts and decomposes rapidly, nearly the whole distilling as a colourless oil, and leaving only a trace of carbonaceous residue. We propose to carefully investigate the products of high boiling point which are formed in the distillation of both the *para*- and *meta*-polymerides of ethylic methylenemalonate.

In his experiments on ethylic methylenemalonate, Zelinsky distilled the *para*-polymeride and obtained thus an oil boiling at 120—210° which he considered to contain ethylic methylenemalonate. By treating this fraction with bromine and subsequent distillation, he isolated an oil boiling at 185—190° (at 75—85 mm.) which, on analysis, gave numbers agreeing approximately with the formula $CH_2Br{\cdot}CBr(COOC_2H_5)_2$. Found Br = 43·67 and 43·99. Theory Br = 48·19 per cent.

Action of Alcoholic Potash on Para-Ethylic Methylenemalonate. Formation of cis-*Tetramethylene*-1 : 3-*dicarboxylic Acid.*

In order, if possible, to obtain some clue to the nature of para-ethylic methylenemalonate, its behaviour towards alcoholic potash was investigated.

Ten grams of the polymeride were added to a solution of 20 grams of potash dissolved in ethylic alcohol and the mixture boiled in a reflux apparatus for 2 hours; water was then added, the clear solution evaporated to dryness on a water bath, to remove all trace of alcohol, and the residue, dissolved in a little water, was acidified and extracted repeatedly with ether; the ethereal solution, dried over calcium chloride, was then evaporated, and the residue heated at 180° in a small retort. This experiment was carefully performed, with a view to determine whether any acrylic acid was produced in this way, but although much carbon dioxide was evolved, practically no acid distilled over during the operation even when the temperature was raised to 220°. It appears, therefore, that no methylenemalonic acid, $CH_2{:}C(COOH)_2$, is formed during the hydrolysis of the polymeride with alcoholic potash, since this acid, if present, should have yielded acrylic acid on heating at 220°.

As soon as the evolution of carbon dioxide had ceased, the residue was dissolved in water, boiled with animal charcoal, filtered, and the concentrated solution allowed to evaporate over sulphuric acid in a vacuum. As no crystals were obtained in this way even after the whole of the water had evaporated, the residue was further purified by very rapidly distilling it under a pressure of 20 mm. On dissolving the colourless, oily distillate in a very little water, saturating the solution with hydrogen chloride, and allowing it to remain for a long time, colourless crystals were deposited, which were collected and further purified by recrystallisation from hydrochloric acid.

The analysis gave the following result.

0·1544 gave 0·2820 CO_2 and 0·0798 H_2O. C = 49·81; H = 5·74.

$C_4H_6(COOH)_2$ requires C = 50·00; H = 5·55 per cent.

This acid melted at 131—132° and showed all the properties of *cis-tetramethylene*-1 : 3-*dicarboxylic acid*; that it was really this acid was shown by converting it into its anhydride which was found to melt at 50—51°, the melting point of the anhydride of the *cis*-acid. The formation of tetramethylenedicarboxylic acid in this way might be taken as evidence that para-ethylic methylenemalonate was ethylic tetramethylenetetracarboxylate, but this is not the case, since the latter ethereal salt is a colourless liquid of quite different properties and shows no tendency to change into a wax-like polymeride.

Examination of the Oil boiling at 250—300° (40 mm.) produced during the Condensation of Formaldehyde with Ethylic Malonate.

In the examination of this oil, it was not found possible to obtain from it by fractional distillation a product of constant boiling point. It was therefore hydrolysed by boiling for 4 hours with an equal weight of pure potash dissolved in alcohol; the product was mixed with water, the solution evaporated until free from alcohol, acidified with hydrochloric acid, and repeatedly extracted with ether. Since, however, the ethereal solution on evaporation deposited only about one-tenth part of the acid which was to have been expected, the aqueous liquors were evaporated to dryness, and the powdered mass extracted with ether in a Soxhlet apparatus. In this way, the required amount of acid was ultimately obtained as a thick syrup, which, even when exposed for some days over sulphuric acid in a vacuum, showed no signs of solidifying. This crude product was heated at 200° in an oil bath until the evolution of carbon dioxide had ceased, and the residue converted into the ethereal salt by treatment with alcohol and sulphuric acid in the usual manner. The ethereal salt, after being well washed with dilute sodium carbonate and dried over calcium chloride, was repeatedly fractionated under reduced pressure; in this way, a considerable fraction was obtained, distilling constantly at 172° (105 mm.), and evidently consisting of nearly pure ethylic tetramethylene-1 : 3-dicarboxylate, the boiling point of which had previously been ascertained to be 173—178° (110 mm.).

This ethereal salt, on hydrolysis in the usual way (see p. 377), yielded a crystalline acid melting at about 130°, which, on analysis, gave the following results.

0·1889 gave 0·3470 CO_2 and 0·095 H_2O. C = 50·1; H = 5·59.

$C_4H_6(COOH)_2$ requires C = 50·00; H = 5·55 per cent.

From this acid, the *silver salt* was obtained as a gelatinous precipitate in the usual manner by precipitating the neutral solution of the ammonium salt with silver nitrate. It gave the following results on analysis.

0·2058 gave 0·1500 CO_2, 0·032 H_2O, and 0·1242 Ag. C = 19·88; H = 1·73; Ag = 60·35.

$C_4H_6(COOAg)_2$ requires C = 20·11; H = 1·68; Ag = 60·31 per cent.

The molecular weight of the acid was determined in acetic acid solution by the cryoscopic method.

I. 0·132 gram of substance dissolved in 32·41 grams of acetic acid caused a depression of 0·11° in the melting point.

II. 0·1463 gram of substance dissolved in 32·41 grams of acetic acid caused a depression of 0·115° in the melting point.

Molecular weight found was I = 144 ; II = 153.

Calculated for $C_6H_8O_4$ = 144.

The properties of this acid indicated that it was *cis*-tetramethylene-1 : 3-dicarboxylic acid, but in order to be sure of this, the remainder of the acid was converted into the anhydride which melted at 50—51°, and was in all respects identical with the anhydride of the *cis*-acid which had previously been obtained.

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THE CONDENSATION OF FORMALDEHYDE WITH ETHYL MALONATE. AND SYNTHESIS OF PENTAMETHYLENE-1:2:4-TRICARBOXYLIC ACID.

BY

J. FRANK BOTTOMLEY

AND

W. H. PERKIN, JUN.

From the Transactions of the Chemical Society, 1900. Vol. 77.

XXVII.—*The Condensation of Formaldehyde with Ethyl Malonate, and Synthesis of Pentamethylene-1 : 2 : 4-tricarboxylic Acid.*

By J. Frank Bottomley and W. H. Perkin, jun.

In a previous communication on the condensation of formaldehyd and ethyl malonate (Haworth and Perkin, Trans., 1898, **73**, 330), it was shown that the following substances were formed either directly or indirectly during this process:

(1) *Ethyl methylenemalonate*, $CH_2{:}C(CO_2Et)_2$, and two polymerides called respectively *ethyl paramethylenemalonate* and *ethyl metamethylenemalonate*.

(2) *Ethyl propanetetracarboxylate*, $(CO_2Et)_2CH{\cdot}CH_2{\cdot}CH(CO_2Et)_2$.

(3) *Ethyl tetramethylenetetracarboxylate*,

$$(CO_2Et)_2C<\begin{matrix}CH_2\\CH_2\end{matrix}>C(CO_2Et)_2.$$

The further investigation of this condensation has again given interesting results, since it has been found that, under conditions different from those used in the first instance, the reaction takes place in such a way that 2 mols. of formaldehyde condense with 3 mols. of ethyl malonate and *ethyl pentanehexacarboxylate* is formed, thus:

$$(CO_2Et_2)_2CH_2 + CH_2O + CH_2(CO_2Et)_2 + CH_2O + CH_2(CO_2Et)_2 = (CO_2Et)_2CH{\cdot}CH_2{\cdot}C(CO_2Et)_2{\cdot}CH_2{\cdot}CH(CO_2Et)_2 + 2H_2O.$$

This new ester, which is solid and melts at 53—55°, is decomposed by boiling with baryta water, with formation of a syrupy polybasic acid which, when heated at 240°, loses carbon dioxide and yields *glutaric acid*.

This curious result may be explained on the assumption that, under the conditions employed, the hexabasic ester, or the hexabasic acid produced from it by hydrolysis, is decomposed into propanetetracarboxylic acid together with methylenemalonic acid or its decomposition products, thus:

$$(CO_2H)_2CH\cdot CH_2\cdot C(CO_2H)_2\cdot CH_2\cdot CH(CO_2H)_2 = (CO_2H)_2CH\cdot CH_2\cdot CH(CO_2H)_2 + CH_2{:}C(CO_2H)_2.$$

The propanetetracarboxylic acid would then, at 240°, lose 2 mols. of carbon dioxide, with formation of glutaric acid.

When, however, ethyl pentanehexacarboxylate is boiled with dilute hydrochloric acid, the hydrolysis proceeds normally, and a syrupy acid is obtained which, on heating at 200°, is decomposed into carbon dioxide and *pentane-aa$_1$γ-tricarboxylic acid*,

$$(CO_2H)_2CH\cdot CH_2\cdot C(CO_2H)_2\cdot CH_2\cdot CH(CO_2H)_2 = 3CO_2 + CO_2H\cdot CH_2\cdot CH_2\cdot CH(CO_2H)\cdot CH_2\cdot CH_2\cdot CO_2H.$$

This acid melts at 113—114·5°, and is doubtless identical with the acid melting at 106—107° which Emery (*Ber.*, 1891, **24**, 284) obtained by hydrolysing ethyl pentanetetracarboxylate,

$$CO_2Et\cdot CH_2\cdot CH_2\cdot C(CO_2Et)_2\cdot CH_2\cdot CH_2\cdot CO_2Et,$$

with alcoholic potash.

Being in possession of considerable quantities of ethyl pentanehexacarboxylate, we have submitted it to careful examination, and as its formula would indicate that it should form a disodium compound of the constitution

$$(CO_2Et)_2CNa\cdot CH_2\cdot C(CO_2Et)_2\cdot CH_2\cdot CNa(CO_2Et)_2,$$

we, in the first place, endeavoured to obtain from it, by the action of sodium ethoxide and methylene iodide, the ethyl hexamethylenehexacarboxylate of the formula

$$(CO_2Et)_2C\begin{<}\begin{matrix}CH_2\cdot C(CO_2Et)_2\\ CH_2\cdot C(CO_2Et)_2\end{matrix}\begin{>}CH_2,$$

which, we have reason to believe, is one of the products formed when formaldehyde condenses with ethyl malonate. It was thought that there would be no difficulty in effecting this synthesis, since it has already been shown (Perkin, Trans., 1891, **59**, 803) that the disodium compound of the analogously constituted ethyl pentanetetracarboxylate, $(CO_2Et)_2CNa\cdot CH_2\cdot CH_2\cdot CH_2\cdot CNa(CO_2Et)_2$, when digested with methylene iodide, yields ethyl hexamethylenetetracarboxylate,

$$(CO_2Et)_2C\begin{<}\begin{matrix}CH_2\text{———}CH_2\\ CH_2\cdot C(CO_2Et)_2\end{matrix}\begin{>}CH_2.$$

Curiously enough, we found that, when digested with sodium ethoxide and methylene iodide in alcoholic solution, or when dissolved in benzene and treated first with sodium and then with methylene iodide, ethyl pentanehexacarboxylate does not appear to yield any ethyl hexamethylenehexacarboxylate, but is entirely split up with formation of large quantities of *ethyl paramethylenemalonate*. This

remarkable result led us to believe that ethyl pentanehexacarboxylate was not capable of forming a disodium compound, but on investigating the point we find that it must yield this derivative, because, when treated in ethereal solution with sodium ethoxide and bromine at a low temperature, it is converted into *ethyl pentamethylenehexacarboxylate*, thus:

$$(CO_2Et)_2C\begin{<}CH_2\cdot C(CO_2Et)_2\\CH_2\cdot C(CO_2Et)_2\end{>}.$$

Possibly the disodium compound is only stable at a low temperature, and when heated to the temperature necessary to enable it to react with methylene iodide, decomposes with formation of 2 mols. of ethyl methylenemalonate and the disodium compound of ethyl malonate, thus:

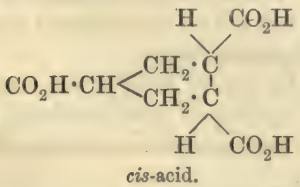
$$(CO_2Et)_2CNa\cdot CH_2\cdot C(CO_2Et)_2\cdot CH_2\cdot CNa(CO_2Et)_2 =$$
$$(CO_2Et)_2C{:}CH_2 + Na_2C(CO_2Et)_2 + CH_2{:}C(CO_2Et)_2.$$

The disodium compound of ethyl malonate would then react with the methylene iodide to form a further quantity of ethyl paramethylenemalonate, and this would account for the large quantity of this ester which is formed when methylene iodide and sodium ethoxide react with ethyl pentanehexacarboxylate.

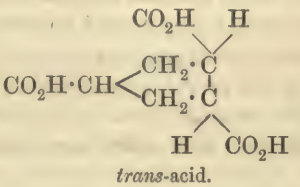
The ethyl pentamethylenehexacarboxylate mentioned above yields on hydrolysis *pentamethylenehexacarboxylic acid*,

$$(CO_2H)_2C\begin{<}CH_2\cdot C(CO_2H)_2\\CH_2\cdot C(CO_2H)_2\end{>},$$

which melts at 210° with evolution of carbon dioxide and formation evidently of a mixture of the *cis*- and *trans*-modifications of *pentamethylenetricarboxylic acid*,



cis-acid.



trans-acid.

The method of preparing and separating these acids is explained on pp. 303—305.

The *trans*-acid appears to melt at 127—130°, but this melting point may be too low, owing to the small amount of material at our disposal and to the very slight tendency to assume a definite crystalline form which this acid exhibits. When the *cis*-modification is heated in a capillary tube, it melts at 146—148°, and if the temperature is raised above this point solidifies again, and the melting point is now found to be 215—217°, a rather striking phenomenon which is due

to the acid being converted into *anhydro*-cis-*pentamethylenetricarboxylic acid*,*

$$CO_2H\cdot CH\begin{<}\begin{matrix}CH_2\cdot CH\cdot CO\\ |\\ CH_2\cdot CH\cdot CO\end{matrix}\end{>}O,$$

with loss of water, a behaviour which is not shown by the *trans*-modification. When treated with acetic anhydride and then distilled, the *cis*-acid also yields the anhydro-acid melting at 215—217°, which on treatment with water is again converted into the *cis*-acid.

The *cis*-acid also differs from the *trans*-acid in forming a calcium salt which is sparingly soluble in cold water. Owing to the interest attaching to the carboxylic acids of pentamethylene, we propose, at a later date, to prepare these *cis*- and *trans*-tricarboxylic acids in larger quantities and to examine them more thoroughly.

During the course of our experiments on the condensation of formaldehyde with ethyl malonate, we gradually accumulated considerable quantities of the wax-like polymeride of ethyl methylenemalonate, which was described in the first communication (*loc. cit.*, p. 340) and which we called ethyl paramethylenemalonate.

We find that this polymeride crystallises well from alcohol, and as, by recrystallisation, we were able to obtain it in a condition slightly purer than the material which was used in our first experiments, we thought it well to repeat some of the remarkable decompositions previously described, and as a result we have been able in all cases to confirm the previous observations.

We find that pure *ethyl paramethylenemalonate* is decomposed on slow distillation almost completely into *ethyl methylenemalonate*, and that this, on standing, is rapidly converted into the horn-like polymeride called *ethyl metamethylenemalonate*. The horn-like polymeride is only very slowly decomposed on heating, but it also is ultimately converted almost quantitatively into *ethyl methylenemalonate*.

In the previous communication (*loc. cit.*, p. 343), it was stated that ethyl paramethylenemalonate, on hydrolysis with alcoholic potash, yielded an acid which was evidently *tetramethylenetetracarboxylic acid*,

$$(CO_2H)_2C\begin{<}\begin{matrix}CH_2\\ CH_2\end{matrix}\end{>}C(CO_2H)_2,$$

since, when heated at 180°, it was converted into cis-*tetramethylene*-1 : 3-*dicarboxylic acid* with loss of carbon dioxide. This synthesis of a tetramethylene ring is, as Michael (*J. pr. Chem.*, 1899, **60**, 438) points out, the only case known of the formation of a 4-carbon ring by

* It has been assumed in the formation of the anhydro-acid, and also in the case of the *cis-trans*-isomerism of the pentamethylenetricarboxylic acids, that the changes occur, as seems likely to be the case, in the succinic, and not in the glutaric, portion of the molecule.

polymerisation of an unsaturated substance. We have repeated these experiments, and can not only confirm the previous observation, but now find that the formation of the tetramethylene compound takes place apparently quantitatively, since we were unable to isolate any other product of the hydrolysis.

Ethyl paramethylenemalonate behaves therefore, on hydrolysis, as if it were the ester of tetramethylenetetracarboxylic acid ; the latter, however, has been prepared, and is an oil which distils without decomposition, that is to say, it has properties quite different from ethyl paramethylenemalonate, which is solid, and on distillation decomposes with formation of ethyl methylenemalonate. In endeavouring to obtain further experimental evidence to explain this difficulty, we have found that freshly distilled ethyl methylenemalonate, if hydrolysed before it has time to polymerise, also yields tetramethylenetetracarboxylic acid. It is very probable that methylenemalonic acid is first produced during these hydrolyses, and, being incapable of existence under the conditions employed, spontaneously polymerises with formation of tetramethylenetetracarboxylic acid,

$$(CO_2H)_2C\overset{CH_2}{\underset{CH_2}{=}}C(CO_2H)_2 \quad = \quad (CO_2H)_2C<\begin{matrix}CH_2\\CH_2\end{matrix}>C(CO_2H)_2.$$

If this explanation is correct, it is certainly remarkable that ethyl methylenemalonate does not polymerise in the same way with formation of ethyl tetramethylenetetracarboxylate. It has, however, been repeatedly shown that this is not the case, and that the product of the polymerisation of the pure ester is the horn-like substance called ethyl metamethylenemalonate.

Experimental.

Preparation of Ethyl Pentanehexacarboxylate, $(CO_2Et)_2CH\cdot CH_2\cdot C(CO_2Et)_2\cdot CH_2\cdot CH(CO_2Et)_2$.

As explained in the introduction, this substance is formed when ethyl malonate is condensed with formaldehyde under certain conditions, and in preparing it we have found the following method give good results.

A flask containing 96 grams of ethyl malonate and 30 grams of a 40 per cent. solution of formaldehyde is well cooled in ice, 1·5 grams of diethylamine then added, and after standing overnight the mixture is heated on a water-bath for 7 hours, and again allowed to stand until the next day. A large quantity of a crystalline product generally separates out, but if this does not happen, the mixture is cooled in a freezing mixture until crystallisation is complete, and the solid product

then separated from adhering oil by filtration on the pump and spreading on porous plates to drain. The oily filtrate, after being separated from the water contained in the formaldehyde solution and formed during the condensation, is distilled under 15 mm. pressure, and the following fractions collected:

100—180°. This consists chiefly of ethyl malonate and ethyl methylenemalonate.

180—210°. This consists chiefly of ethyl propanetetracarboxylate.

210—260°. This fraction, on standing, deposits crystals of ethyl pentanehexacarboxylate, which are separated from the oily impurity in the way explained above.

The yield obtained with the quantities of material stated above are approximately as follows:

Ethyl paramethylenemalonate	3 grams.
Ethyl pentanetetracarboxylate	25 „
Ethyl propanehexacarboxylate	48 „
Oils of high boiling point	10 „

During the course of a number of experiments which were instituted with the object of determining the conditions under which ethyl pentanetetracarboxylate is formed, it was found that the amount of diethylamine used had a very appreciable effect on the yield of this substance. Using 96 grams of ethyl malonate and 30 grams of formaldehyde solution in each case, the following results were obtained with varying quantities of diethylamine:

Diethylamine used	0·5	1·0	1·5 grams.
Ethyl pentanehexacarboxylate formed	32	43	48 „

Ethyl pentanehexacarboxylate crystallises from 70 per cent. alcohol in long, silky needles, and is very soluble in alcohol, ether, benzene, or glacial acetic acid. It melts at 53—55°, and distils almost without decomposition at 254—256° under 15 mm. pressure. On analysis:

0·1767 gave 0·3573 CO_2 and 0·1141 H_2O. C = 55·16; H = 7·17.
0·1842 „ 0·3729 CO_2 „ 0·1182 H_2O. C = 55·20; H = 7·13.
$C_{23}H_{36}O_{12}$ requires C = 54·75; H = 7·14 per cent.

Hydrolysis of Ethyl Pentanehexacarboxylate by means of Hydrochloric Acid. Formation of Pentanetricarboxylic Acid, $CO_2H\cdot CH_2\cdot CH_2\cdot CH(CO_2H)\cdot CH_2\cdot CH_2\cdot CO_2H$.

This hydrolysis, which proceeds normally, was conducted as follows. Ethyl pentanehexacarboxylate, in portions of 5 grams, was boiled on a sand-bath with a mixture of 10 grams of concentrated hydrochloric acid and 10 grams of water. After the boiling had been

continued for about 15 hours, and the oil had completely disappeared, the liquid was evaporated on the water-bath to a thick syrup, when it was noticed that carbon dioxide was given off in some quantity towards the end of the evaporation. The syrup was heated in a small flask in a paraffin bath at 200° until the evolution of carbon dioxide had ceased, the residue was then dissolved in water and boiled for some time with carefully purified animal charcoal. After filtering, the solution was concentrated, allowed to stand over sulphuric acid in a vacuum desiccator until a crystalline cake had formed, and the solid mass, which melted at 100—110°, further purified by crystallisation from a mixture of acetone and chloroform. *Pentanetricarboxylic acid* melts at 113—114·5°. On analysis:

0·1520 gave 0·2604 CO_2 and 0·0802 H_2O. C = 46·73; H = 5·86.
$C_8H_{12}O_6$ requires C = 47·05; H = 5·88 per cent.

The *silver* salt, $C_8H_9O_6Ag_3$, was obtained, on adding silver nitrate to the neutral solution of the ammonium salt, as a white, amorphous precipitate, which was analysed with the following result:

0·1627 gave, on ignition, 0·1 Ag. Ag = 61·48.
$C_8H_9O_6Ag_3$ requires Ag = 61·7 per cent.

As already stated in the introduction, this acid is probably identical with Emery's pentanetricarboxylic acid melting at 106—107°.

Action of Baryta on Ethyl Pentanehexacarboxylate. Formation of Glutaric Acid.

In carrying out this curious decomposition, 40 grams of recrystallised ethyl pentanehexacarboxylate were boiled with an excess of baryta for about 6 hours. The thick, sparingly soluble barium salt which had separated was collected, washed with hot water, and carefully decomposed with dilute sulphuric acid, any slight excess of the acid being removed by adding small quantities of the barium salt, until the filtrate gave no precipitate with barium chloride. The barium sulphate was then filtered off and the solution evaporated on the water-bath, when a thick syrup was obtained which was transferred to a small flask and heated in an oil-bath at 240° until carbon dioxide ceased to be given off. The residue, which solidified on cooling, was dissolved in water, boiled with animal charcoal, and the solution, after filtration, evaporated on a water-bath to the consistency of a thick syrup.

On standing for some time in a vacuum desiccator, the syrup crystallised, and after spreading on a porous plate a white residue was obtained which crystallised well from benzene, melted at 94—96°, and had all the properties of glutaric acid. Analysis:

0·1635 gave 0·2723 CO_2 and 0·0946 H_2O. C = 45·42; H = 6·43.
$C_5H_8O_4$ requires C = 45·50; H = 6·07 per cent.

A small quantity of this acid was mixed with another specimen of glutaric acid, and the melting point of the mixed samples was found to be 94—96°. Another portion was neutralised with ammonia and a solution of zinc chloride added, when, on boiling, the characteristic zinc salt of glutaric acid separated.

Action of Sodium Ethoxide and Methylene Iodide on the Disodium Compound of Ethyl Pentanehexacarboxylate. Attempt to prepare Ethyl Hexamethylenehexacarboxylate.

This experiment was carried out in two ways, namely, in alcoholic and in benzene solution:

I. Ethyl pentanehexacarboxylate (20 grams) was added to a solution of 1·85 grams of sodium in absolute alcohol; the whole was then heated on a water-bath in a reflux apparatus, and 10·6 grams of methylene iodide added, the flask being well shaken to promote thorough solution. After boiling for about 9 hours, the mixture, which was practically neutral, was freed as far as possible from alcohol by heating on the water-bath, water was then added, and the oil extracted with ether. The ethereal solution was washed well, dried with calcium chloride, the ether distilled off, and the oily residue fractionated under 15 mm. pressure. After a small quantity of unchanged methylene iodide had distilled over, the temperature rose rapidly to 120°, and a fraction was collected up to 167°, the greater part of which distilled between 150° and 167°. A small quantity came over between 200° and 248°, after which decomposition set in. The fraction 120—167°, on standing, became warm and solidified to a waxy mass which had exactly the appearance of ethyl paramethylenemalonate, and after recrystallising from absolute alcohol melted at 148—150°. Further investigation showed conclusively that this substance, which was obtained in considerable quantity, was ethyl paramethylenemalonate.

II. 10 grams of ethyl pentanehexacarboxylate were dissolved in about 600 c.c. of dry benzene, and to this solution 0·92 gram of sodium, which had previously been brought into a state of very fine division by melting under boiling xylene and shaking vigorously, was added. The mixture was then heated on the water-bath until all but the merest trace of the sodium had dissolved and a sticky mass of a sodium compound had begun to separate out on the sides of the flask. 5·3 grams of methylene iodide were then added, and the heating continued for some hours, when a copious precipitate of sodium iodide was deposited. After standing overnight, the benzene was distilled off and the residue treated as before. In this way, 10 grams of an

oil were obtained nearly all of which distilled between 135° and 145° under 15 mm. pressure, and soon solidified to a hard cake of ethyl paramethylenemalonate.

The formation of ethyl paramethylenemalonate in this way is very remarkable, and seems to show that it is not possible to prepare ethyl hexamethylenehexacarboxylate by the action of methylene iodide on the disodium compound of ethyl pentanehexacarboxylate.

Pentamethylenehexacarboxylic Acid, $(CO_2H)_2C<\begin{matrix}CH_2\cdot C(CO_2H)_2\\ CH_2\cdot C(CO_2H)_2\end{matrix}$.

The ester of this interesting acid is obtained when bromine acts on the disodium compound of ethyl pentanehexacarboxylate.

Sodium (1·83 grams) is dissolved in as small a quantity of absolute alcohol as possible, and the ethoxide, while still hot, is mixed with twice its volume of dry ether and, after cooling with ice, gradually added to an ethereal solution of ethyl pentanehexacarboxylate (20 grams). Bromine is then allowed to drop in slowly, with constant shaking, until the mixture has attained a light straw colour, all rise of temperature being carefully avoided. After standing for half an hour, the ethereal solution is well washed with water, dried over calcium chloride, and the ether distilled off, when a thick oil remains which, on distillation under 15 mm. pressure, yielded two fractions boiling at 190—215° and 230—245° respectively. During the distillation a considerable amount of decomposition took place.

The fraction boiling at 190—215° was hydrolysed by boiling with an excess of baryta, the insoluble barium salt collected on the pump, well washed, mixed with boiling water, and decomposed exactly with sulphuric acid. After filtering from barium sulphate and evaporating the filtrate slowly on the water-bath, a thick syrup resulted which, on standing, partially crystallised. This crude product was left in contact with porous earthenware for some days until quite dry, and the hard, colourless mass thus obtained recrystallised from glacial acetic acid. The colourless crystals melted at 210—212° with decomposition, and evidently consisted of *pentamethylenehexacarboxylic acid*. On analysis:

0·1509 gave 0·2147 CO_2 and 0·0393 H_2O. C = 38·81 ; H = 2·89.

$C_{11}H_{10}O_{12}$ requires C = 39·49 ; H = 2·99 per cent.

A silver salt was prepared in the usual way, but in attempting to determine the silver by heating in a crucible, the salt decomposed almost with explosive violence, being scattered out of the crucible. It was therefore decomposed by heating slowly to 250° in an air-bath and then igniting the residue in the usual way. The results obtained were

about 5 per cent. too low, showing that the silver salt was a mixture of the neutral salt with considerable quantities of acid salts. Similar difficulties have been observed in other cases in attempting to prepare pure neutral silver salts of polybasic acids.

Preparation of Trimethyl Pentamethylenetricarboxylate,

$$CO_2Me\cdot CH<\begin{matrix}CH_2\cdot CH(CO_2Me)\\ CH_2\cdot CH(CO_2Me)\end{matrix}.$$

The yield of pure pentamethylenehexacarboxylic acid obtained by the method described in the last section was too small to allow of the tricarboxylic acids obtained from it by the elimination of carbon dioxide being examined in detail. We, however, ultimately found that the trimethyl ester of these acids could be prepared direct from the product of the action of bromine on the sodium compound of ethyl pentanehexacarboxylate in the following way.

Ethyl pentanehexacarboxylate (100 grams) was treated as before with sodium ethoxide and bromine, and the crude product hydrolysed by boiling it with an excess of caustic potash dissolved in methyl alcohol. After the hydrolysis was complete, the bulk of the methyl alcohol was distilled off, water was then added, and the solution evaporated to remove the last traces of the alcohol. The concentrated solution was then acidified with excess of hydrochloric acid, evaporated to dryness, the residue mixed with sand and extracted for three days with pure ether in a Soxhlet apparatus. After distilling off the ether, the residual syrupy acid was heated in a paraffin-bath at 200° until carbon dioxide ceased to be given off, the sticky, dark-coloured mass mixed with 150 grams of methyl alcohol, then with 50 grams of concentrated sulphuric acid, and the whole heated for 7 hours on the water-bath. After standing overnight, the product was diluted with water and extracted several times with ether; the ethereal solution was then washed with water and dilute sodium carbonate, dried over anhydrous sodium sulphate, and the ether distilled off. The residual oil was fractionated under 15 mm. pressure, when two principal fractions were obtained boiling at 100—130° and 167—170°, which, after repeated refractionation, boiled ultimately at 207—212° under 760 mm., and at 164—166° under 12 mm. pressure respectively. The latter consisted of trimethyl pentamethylenetricarboxylate, as the following analysis shows:

0·2018 gave 0·3977 CO_2 and 0·1208 H_2O. C = 53·75; H = 6·65.

$C_{11}H_{16}O_6$ requires C = 54·1; H = 6·57 per cent.

The oil boiling at 207—212° was also analysed, but the result gave no clue as to its constitution. On hydrolysis, it yielded a mixture of

acids which, by crystallisation, was roughly separated into two parts melting at 85—95° and 105—115° respectively. It seems likely that this mixture consisted of glutaric acid and tetramethylenedicarboxylic acid, but the quantity was too small for further examination.

trans-*Pentamethylenetricarboxylic Acid*, $CO_2H \cdot CH<\begin{matrix}CH_2 \cdot C(CO_2H)(H)\\CH_2 \cdot C(H)(CO_2H)\end{matrix}$

In preparing this acid, the trimethyl ester described in the last section was hydrolysed by boiling with excess of methyl alcoholic potash, water was then added, the methyl alcohol removed by evaporation on the water-bath, and the residue acidified with hydrochloric acid. After saturating with ammonium sulphate, the solution was extracted with pure ether, an operation which had to be repeated forty times before the whole of the acid was removed. The ethereal solution was then dried over anhydrous sodium sulphate, the ether distilled off, and the residue allowed to stand in a desiccator over sulphuric acid until it had completely solidified. In this way, 14 grams of a solid acid melting at 115—125°, and which was probably a mixture of the *cis*- and *trans*-modification of pentamethylenetricarboxylic acid, was obtained from 17 grams of the trimethyl ester. Unfortunately, this mixture is very difficult to crystallise, but ultimately repeated recrystallisation from concentrated hydrochloric acid yielded an acid which melted at 127—130° and was analysed with the following results:

0·1458 gave 0·2549 CO_2 and 0·0669 H_2O. C = 47·66; H = 5·1.

$C_8H_{10}O_6$ requires C = 47·5; H = 4·95 per cent.

This acid differs from *cis*-pentamethylenetricarboxylic acid described on p. 305, as it is not converted into an anhydro-acid melting at 217° when heated at 150—160°, and moreover forms a calcium salt which is soluble in cold water and precipitated on boiling the solution. We assume therefore that it is trans-*pentamethylenetricarboxylic acid*. When larger quantities have been prepared, it is possible that the melting point will be found to be higher than that given above.

Anhydro-cis-*pentamethylenetricarboxylic Acid*,

$CO_2H \cdot CH<\begin{matrix}CH_2 \cdot CH \cdot CO\\CH_2 \cdot CH \cdot CO\end{matrix}>O.$

This well characterised substance was prepared in the following way. Crude pentamethylenetricarboxylic acid melting at 115—125°

was dissolved in four times its weight of acetic anhydride and boiled in a reflux apparatus for 2 hours. The whole was then transferred to a fractionating flask, and after the acetic anhydride had been distilled off at the ordinary pressure, the residue was distilled *as rapidly as possible* under 15 mm. pressure. A great deal of decomposition took place, but a considerable quantity of an oily distillate was nevertheless obtained, which, on cooling, solidified to distinct crystals mixed with some dark coloured impurity. The product was dissolved in a mixture of acetone and chloroform, the solution boiled with purified animal charcoal, and allowed to stand for some time, when crystals separated which, after twice recrystallising, were almost colourless. On analysis:

0·1360 gave 0·2592 CO_2 and 0·0585 H_2O. C = 51·98; H = 4·78.
$C_8H_8O_5$ requires C = 52·17; H = 4·34 per cent.

Anhydro-cis-*pentamethylenetricarboxylic acid* melts at 215—217°, and although it dissolves only sparingly in cold water, is sufficiently soluble to form a distinctly acid solution; it dissolves readily in boiling water and in cold dilute sodium carbonate solution.

cis-*Pentamethylenetricarboxylic acid*, $CO_2H\cdot CH<\begin{matrix}CH_2\cdot C(H)(CO_2H)\\ CH_2\cdot C(H)(CO_2H)\end{matrix}$.

This acid is formed by the action of water on anhydro-*cis*-pentamethylenetricarboxylic acid. 0·5 gram of the pure, finely powdered anhydro-acid was boiled for about an hour with water, and the solution evaporated on the water-bath until the acid began to crystallise out. After standing overnight in a vacuum desiccator, the crystals were spread on a porous plate, dried over sulphuric acid, and analysed, with the following result:

0·1519 gave 0·2643 CO_2 and 0·0700 H_2O. C = 47·45; H = 5·12.
$C_8H_{10}O_6$ requires C = 47·52; H = 4·95 per cent.

cis-Pentamethylenetricarboxylic acid melts at 146—148°; at 150—160° it splits off water and solidifies, melting again at 215—217°, the melting point of the anhydro-acid. The calcium salt of this acid differs from that of the *trans*-derivative in being insoluble in cold water.

*Preparation of Ethyl Paramethylenemalonate.**

The method employed for the preparation of this polymeride of ethyl methylenemalonate was practically the same as that described on p. 298 for the production of ethyl pentanehexacarboxylate, with the exception that the proportion of ethyl malonate and formaldehyde employed was different. As the result of several experiments, it was found that the best results were obtained by using 96 grams of ethyl malonate, 45 grams of 40 per cent. formaldehyde solution, and 1·5 grams of diethylamine.

After the condensation was complete, the product was distilled under 35 mm. pressure, and the following fractions collected:

I. 120—190°. II. 190—230°. III. 230—270°

The fraction 120—190° became warm on standing and slowly solidified to a waxy solid. This was spread on porous plates to remove adherent oil and crystallised from absolute alcohol, when pure ethyl paramethylenemalonate separated in the form of a colourless crystalline powder melting at 154—156°. The best yield obtained in this way was 22 grams of the crude dry product before crystallisation, but for some reason the yield varies very much in different operations, although the greatest care may be taken to reproduce in each case the same conditions.

Hydrolysis of Ethyl Paramethylenemalonate with Alcoholic Potash. Formation of cis-*Tetramethylenedicarboxylic Acid,*

$$CO_2H\cdot CH<\begin{matrix}CH_2\\CH_2\end{matrix}>CH\cdot CO_2H.$$

This hydrolysis, which has already been described (Trans., 1898, **73** 343), was repeated for reasons stated in the introduction to this paper. Carefully recrystallised ethyl paramethylenemalonate (20 grams) was boiled with a solution of 25 grams of caustic potash in methyl alcohol for about an hour. The methyl alcohol was distilled off as far as possible, water was then added, the solution boiled to remove the last traces of methyl alcohol, acidified with excess of hydrochloric acid, evaporated to dryness, and the solid residue, after mixing with sand, extracted in a Soxhlet apparatus with pure ether. The acid which remained, after distilling off the ether, was heated in a small flask at 200° until carbon dioxide ceased to be given off. The residue, which

* By an unfortunate mistake, the amount of diethylamine used was omitted in the previous description of the condensation of formaldehyde with ethyl malonate (Trans., 1898, **73**, 339); the amount used at that time was about 3 grams for the quantities of formaldehyde and ethyl malonate stated.

solidified on cooling, was dissolved in water, boiled with animal charcoal, filtered, and the filtrate concentrated and saturated with hydrogen chloride; nothing, however, separated until the solution was placed over solid potash in a vacuum desiccator, and then crystals gradually formed which melted at 131—132°, and consisted of *tetramethylene-1 : 3-dicarboxylic acid.* On analysis:

0·1459 gave 0·2678 CO_2 and 0·0748 H_2O. C = 50·05; H = 5·69.
$C_6H_8O_4$ requires C = 50·0; H = 5·55 per cent.

The amount of the acid obtained in this way was not actually determined, but it was considerable, and on carefully examining the mother liquors, we were unable to detect the presence of any other substance. This experiment confirms, therefore, the results obtained under different conditions on the former occasion.

Distillation of Ethyl Paramethylenemalonate. Formation of Ethyl Methylenemalonate and of Ethyl Metamethylenemalonate.

The distillation of ethyl paramethylenemalonate has already been described (Trans., 1898, 73, 341), but as the small amount of material employed had not been recrystallised, and as the distillation was conducted under the ordinary pressure, it was thought necessary to repeat the experiments with pure material on a larger scale and under different conditions. Pure recrystallised ethyl paramethylenemalonate (15 grams) was slowly distilled under 35 mm. pressure from an ordinary fractionating flask, when practically the whole passed over below 220°, two fractions, boiling respectively at 140—190° and 190—210°, being collected. It was noticed, especially during the early stages of the distillation, that a gas appeared to be given off, and that white fumes were formed which did not condense.

The fraction 140—190°, which had an irritating odour resembling that of formaldehyde, was immediately redistilled under the ordinary pressure, when nearly the whole of it passed over between 205° and 210°, and this, on standing, soon became quite warm and polymerised to the horny modification called *ethyl metamethylenemalonate.*

The fraction boiling at 190—210° under 35 mm. pressure was then examined, and on refractionation was found to distil almost completely between 110° and 120° under 30 mm. pressure, a result which seems to indicate that the liquid boiling at 190—210° under 35 mm. pressure still contained some ethyl paramethylenemalonate which had escaped decomposition during the first distillation. The boiling point, 110—120° under 30 mm. pressure, is approximately that of ethyl methylenemalonate, and since the fraction readily decolorised bromine,

there can be no doubt that it contained considerable quantities of this ester. It remained, however, as a perfectly mobile liquid for nearly a fortnight, which is remarkable, since ethyl methylenemalonate generally polymerises within a few minutes, and it would therefore appear that slight impurities are capable of arresting this polymerisation. On the addition of a small crystal of ethyl paramethylenemalonate to the oil, polymerisation commenced at once, but, curiously enough, the polymeride formed was the *meta*- and not the para-modification.

The remainder of the liquid was redistilled under atmospheric pressure, when nearly the whole passed over between 202° and 210°, but towards the end of the distillation the liquid in the fractionating flask became very thick, and seemed to polymerise. The distillate, on standing, polymerised to ethyl metamethylenemalonate, but before this took place a small quantity was analysed:

0·1748 gave 0·3534 CO_2 and 0·1077 H_2O. C = 55·14; H = 6·85.
$CH_2{:}C(CO_2Et)_2$ requires C = 55·81; H = 6·98 per cent.

This result confirms the statement made in the previous communication (*loc. cit.*, p. 341), that ethyl paramethylenemalonate, on distillation, is resolved into the methylenemalonate, $CH_2{:}C(CO_2Et)_2$.

Distillation of Ethyl Metamethylenemalonate, and Hydrolysis of Ethyl Methylenemalonate.

After the results obtained in the distillation of ethyl paramethylenemalonate, it seemed interesting to investigate the *meta*-polymeride in the same direction.

Ethyl metamethylenemalonate, which was so tough and hard that it had to be broken up with a knife and hammer, was very slowly distilled in a small fractionating flask under 32 mm. pressure, using a small air-bath to heat the flask. During the distillation, some white fumes were given off which did not condense. The whole distilled over between 110° and 120° leaving no residue, and on refractionating the distillate under the ordinary pressure, almost all boiled between 204° and 210°, but towards the end of the operation the small residue in the flask became very thick, and polymerisation seemed to be taking place. The oil boiling at 204—210° was found to consist of ethyl methylenemalonate, showing that the meta-, like the para-polymeride, is, on distillation, resolved into simple molecules of the composition $CH_2{:}C(CO_2Et)_2$. The bulk of the ethyl methylenemalonate obtained in this way was at once, and before it had had time to polymerise, mixed with excess of alcoholic potash and heated on the water-bath until hydrolysis was complete. After evaporating off the alcohol, the residue was dissolved in hydrochloric acid and extracted repeatedly with ether; the ether

was distilled off and the residual syrup rapidly distilled at the ordinary pressure. Almost the whole passed over between 250° and 270° and partially solidified, and after crystallisation from hydrochloric acid, colourless crystals were obtained which melted at 132—134°. On analysis:

0·1023 gave 0·1901 CO_2 and 0·0530 H_2O. C = 50·67; H = 5·75.
$C_6H_8O_4$ requires C = 50·05; H = 5·55 per cent.

Examination of this acid showed that it was *cis*-tetramethylenedicarboxylic acid, and its formation seems to indicate that methylenemalonic acid is not capable of existence under the conditions mentioned above, but at once undergoes polymerisation.

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RICHARD CLAY AND SONS, LIMITED, LONDON AND BUNGAY

TETRAMETHYLENECARBINOL.

BY

W. H. PERKIN, JUN.

From the Transactions of the Chemical Society, 1901. Vol. 79

XXXIV.—*Tetramethylenecarbinol.*

By W. H. Perkin, jun.

During the course of an investigation on *hydroxytetramethylene*,

$$\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CH\cdot OH\end{matrix}$$

(Trans., 1894, **65**, 960), it was thought that it would be interesting to compare the properties of this substance with those of an alcohol derived from tetramethylene but containing the hydroxyl group outside the ring, and for this reason experiments were made on the reduction of the chloride of tetramethylenecarboxylic acid, in the hope that it might prove possible to prepare tetramethylenecarbinol in quantity by this means:

$$\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CH\cdot COCl\end{matrix} + 4H = \begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CH\cdot CH_2OH\end{matrix} + HCl.$$

The result of these experiments showed that, although the reduction does proceed in this way, the yield of tetramethylenecarbinol produced is so small that a sufficiently detailed examination of its behaviour with reagents would be very difficult. It was prepared as follows.

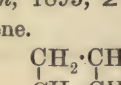
Pure ether was shaken with water until thoroughly wet and then placed on a layer of 25 per cent. caustic soda solution contained in a bottle fitted with a wide reflux condenser and standing in running water. Sodium (10 grams) cut into small pieces, was introduced all at once, and then through the top of the condenser a solution of 5 grams of tetramethylenecarboxylic chloride was run in moderately rapidly.

The ethereal solution from five such experiments was washed with dilute hydrochloric acid, the ether distilled off, and the residual oil, which smelt of tetramethylenealdehyde, and which had no constant boiling point, was boiled for one hour with methyl alcoholic potash in order to decompose the tetramethylenecarboxylic ester of tetramethylenecarbinol, which was evidently one of the substances formed in the reaction.

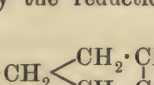
The alkaline solution was mixed with water, extracted with ether,* and the ethereal solution washed with dilute hydrochloric acid and dried over anhydrous potassium carbonate. On distilling off the ether, a small quantity of a colourless oil was obtained, which after twice fractionating distilled constantly at 143—144° under 760 mm. pressure. On analysis:

0·1912 gave 0·4872 CO_2 and 0·2026 H_2O. C = 69·5; H = 11·8.
0·1721 „ 0·4392 CO_2 „ 0·1818 H_2O. C = 69·6; H = 11·7.
$C_5H_{10}O$ requires C = 69·7; H = 11·6 per cent.

Tetramethylenecarbinol is a colourless oil which smells like amyl alcohol, and is somewhat soluble in water. It is isomeric with pentamethenyl alcohol, boiling at 139°, which Wislicenus and Hentschel (*Annalen*, 1893, 275, 322) obtained by the reduction of ketopentamethylene.



Tetramethylenecarbinol.



Pentamethenyl alcohol.

The determinations of the density, magnetic rotation and refractive power of tetramethylenecarbinol were carried out by W. H. Perkin, sen., with the following results:

Density: 4°/4° = 0·9162; 15°/15° = 0·9088; 25°/25° = 0·9029.

* By acidifying the alkaline solution and extracting with ether, almost the whole of the unreduced tetramethylenecarboxylic acid may be recovered.

Magnetic rotation.

t.	Sp. rotation.	Mol. rotation.
16·7°	1·0098	5·314.

The probable rotation of a substance of this composition may be calculated from the values of the elements thus:

$$\begin{aligned} C_5 &= 0{\cdot}515 \times 5 = 2{\cdot}575 \\ H_{10} &= 0{\cdot}254 \times 10 = 2{\cdot}540 \\ O \text{ (as in alcohols)} &= 0{\cdot}194 \end{aligned}$$

Cal. rotation of tetramethylenecarbinol = 5·309

The number thus obtained agrees well with that actually found.

Refractive power.

$d\ 8{\cdot}7°/8{\cdot}7° = 0{\cdot}9128.$

	$\mu\ 8{\cdot}7°.$	$\frac{\mu-1}{d}$.	$\frac{\mu-1}{d}p$.
K	1·44096	0·48308	41·544
H_α	1·44368	0·48606	41·801
Na	1·44608	0·48869	42·027
H_β	1·45187	0·49504	42·573
H_γ	1·45645	0·50005	43·005

The calculated refractive power for H_α is obtained thus:

$$\begin{aligned} C_5 &= 25{\cdot}00 \\ H_{10} &= 13{\cdot}00 \\ O \text{ (as in alcohols)} &= 2{\cdot}80 \\ C_5H_{10}O &= 40{\cdot}80 \end{aligned}$$

The value found is greater than that calculated by no less than 1·0, whereas ring compounds usually give a refractive power which is only 0·29 higher than that calculated in the above way.

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THE ACTION OF ETHYLENE DIBROMIDE AND TRIMETHYLENE DIBROMIDE ON THE SODIUM COMPOUND OF ETHYLIC CYANACETATE.

BY

H. C. H. CARPENTER

AND

WILLIAM HENRY PERKIN, JUN.

From the Transactions of the Chemical Society, 1899.

The Action of Ethylene Dibromide and Trimethylene Dibromide on the Sodium Compound of Ethylic Cyanacetate.

By H. C H. Carpenter and W. H. Perkin, jun.

In investigating the derivatives of tri- and tetra-methylene, one of the greatest difficulties met with was the smallness of the yield obtained in the reactions employed in their preparation; thus the amount of ethylic trimethylenedicarboxylate produced by the action of ethylene dibromide on the sodium compound of ethylic malonate

is seldom more than 10 per cent. of the theoretical. During the course of some researches on the action of the ethereal salts of unsaturated acids on ethylic malonate, it was found that the yield of condensation product was very largely increased when ethylic cyanacetate was substituted for ethylic malonate (compare Perkin and Thorpe, Trans., 1899, **75**, 50), and this led us to institute experiments with the object of determining whether a similar increase in the yield might not be obtained by allowing ethylene dibromide and trimethylene dibromide to react with the sodium compound of ethylic cyanacetate in place of ethylic sodiomalonate; this has been found to be the case.

When the sodium compound of ethylic cyanacetate, suspended in alcohol, is digested with ethylene dibromide, the reaction proceeds normally with formation of ethylic cyanotrimethylenecarboxylate,

$$2NaCH(CN)\cdot COOC_2H_5 + BrCH_2\cdot CH_2Br = \begin{matrix}CH_2\\ |\\ CH_2\end{matrix}\!\!>C(CN)\cdot COOC_2H_5 + CH_2(CN)\cdot COOC_2H_5 + 2NaBr,$$

and the yield of this substance is over 50 per cent. of the theoretical.

This ethereal salt, which is a colourless oil boiling at 210—211°, is easily hydrolysed by alcoholic potash, yielding in the first place a crystalline acid, $C_5H_5NO_2$, which melts at 149°, gives a silver salt of the formula $C_5H_4AgNO_2$, and thus is apparently *cyanotrimethylenecarboxylic acid*, $\begin{matrix}CH_2\\ |\\ CH_2\end{matrix}\!\!>C(CN)\cdot COOH$.

When this acid is heated, it sublimes to some extent unchanged, but the bulk of it decomposes with much charring and without the formation of cyanotrimethylene, $\begin{matrix}CH_2\\ |\\ CH_2\end{matrix}\!\!>CH\cdot CN$. Since, under similar conditions, the corresponding *cyanotetramethylenecarboxylic acid*, $\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot C(CN)\cdot COOH\end{matrix}$ (p. 932), is almost quantitatively converted into carbon dioxide and cyanotetramethylene, it seemed doubtful whether the two acids could be analogously constituted, and we were therefore for some time of the opinion that the substance described as cyanotrimethylenecarboxylic acid might in reality be the isomeric *imide* of trimethylenedicarboxylic acid, $\begin{matrix}CH_2\\ |\\ CH_2\end{matrix}\!\!>C<\begin{matrix}CO\\ CO\end{matrix}\!\!>NH$, a substance which would also give a silver salt of the formula $C_5H_4NO_2Ag$. The solution of the substance in water, however, is strongly acid to litmus, and readily decomposes carbonates, properties which would hardly be shown by an imide; we have therefore assumed in this paper that it is cyanotrimethylenecarboxylic acid, and additional experiments will be made with the object of obtaining further information

in explanation of the remarkable difference in properties exhibited by this acid and cyanotetramethylenecarboxylic acid.

When cyanotrimethylenecarboxylic acid is hydrolysed by boiling with excess of aqueous potash, it is converted into trimethylenedicarboxylic acid, $\begin{matrix}CH_2\\|\\CH_2\end{matrix}>C(COOH)_2$, consequently this acid, which formerly could be obtained only in small quantity by starting with ethylic malonate, is now a substance comparatively easy of preparation.

When ethylene dibromide reacts with the sodium compound of ethylic malonate, there is always produced, besides ethylic trimethylenedicarboxylate, a small quantity of ethylic butanetetracarboxylate,

$$2CHNa(COOC_2H_5)_2 + BrCH_2\cdot CH_2Br = (COOC_2H_5)_2CH\cdot CH_2\cdot CH_2\cdot CH(COOC_2H_5)_2 + 2NaBr,$$

the latter being easily separated from the former by distillation in steam. When ethylic cyanacetate is substituted for ethylic malonate in this reaction, a similar behaviour was noticed, as on distilling the product in steam, a quantity of oil was left in the distillation flask, and on cooling solidified. This substance which crystallises from alcohol in glistening prisms (m. p. 119·5°), gives, on analysis, numbers agreeing with those required for the formula $C_9H_{12}N_2O_4$, and since, on hydrolysis, it is almost quantitatively converted into adipic acid, its constitution is evidently represented by the formula $CN\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(CN)\cdot COOC_2H_5$, which is that of *ethylic aδ-dicyanovalerate*. The formation of this substance is somewhat remarkable, and may be assumed to take place in two stages. In the first place, ethylic dicyanobutanedicarboxylate is produced,

$$2NaCH(CN)\cdot COOC_2H_5 + BrCH_2\cdot CH_2Br = COOC_2H_5\cdot CH(CN)\cdot CH_2\cdot CH_2\cdot CH(CN)\cdot COOC_2H_5 + 2NaBr,$$

and from this ethereal salt, by partial hydrolysis and elimination of carbon dioxide, ethylic dicyanovalerate is produced,

$$COOC_2H_5\cdot CH(CN)\cdot CH_2\cdot CH_2\cdot CH(CN)\cdot COOC_2H_5 + H_2O = CO_2 + C_2H_5\cdot OH + CN\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(CN)\cdot COOC_2H_5.$$

This substance should form a sodium compound which, by treatment with alkyl iodides, &c., and subsequent hydrolysis and elimination of carbonic anhydride, should yield *mono*-substituted adipic acids, a synthesis which would be of much value, since these acids are, at the present time, exceedingly difficult to prepare.

When the sodium compound of ethylic cyanacetate is mixed with alcohol and trimethylene dibromide, a vigorous reaction takes place, and ethylic cyanotetramethylenecarboxylate is formed thus:

$$2NaCH(CN)\cdot COOC_2H_5 + BrCH_2\cdot CH_2\cdot CH_2Br = \begin{matrix} CH_2\cdot CH_2 \\ | \quad | \\ CH_2\cdot C(CN)\cdot COOC_2H_5 \end{matrix} + CH_2(CN)\cdot COOC_2H_5 + 2NaBr.$$

The ethereal salt, of which a very good yield is obtained in this way, is, on hydrolysis, first converted into the corresponding *cyanotetramethylenecarboxylic acid*, $\begin{matrix} CH_2\cdot CH_2 \\ | \quad | \\ CH_2\cdot C(CN)\cdot COOH \end{matrix}$ (m. p. 69°), and this, on boiling with aqueous potash, yields tetramethylenedicarboxylic acid, $\begin{matrix} CH_2\cdot CH_2 \\ | \quad | \\ CH_2\cdot C(COOH)_2 \end{matrix}$.

When cyanotetramethylenecarboxylic acid is carefully heated, it sublimes unchanged; but if slowly distilled, it decomposes completely with evolution of carbon dioxide and formation of *cyanotetramethylene*, $\begin{matrix} CH_2\cdot CH_2 \\ | \quad | \\ CH_2\cdot CH\cdot CN \end{matrix}$. This interesting substance is a colourless oil boiling at 148—149°, which, on hydrolysis, is quantitatively converted into tetramethylenecarboxylic acid, $\begin{matrix} CH_2\cdot CH_2 \\ | \quad | \\ CH_2\cdot CH\cdot COOH \end{matrix}$.

In the reaction between the sodium compound of ethylic cyanacetate and trimethylene dibromide, an oily substance is formed which is not volatile in steam, and decomposes on distillation. Since this oil, on hydrolysis, yields pimelic acid, it is evidently either ethylic dicyanopentanedicarboxylate,

$$COOC_2H_5\cdot CH(CN)\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(CN)\cdot COOC_2H_5,$$

or ethylic $\alpha\epsilon$-dicyanocaproate,

$$CN\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(CN)\cdot COOC_2H_5,$$

and experiments are in progress with the object of determining its constitution.

Experimental.

Action of Ethylene Dibromide on Ethylic Sodiocyanacetate. Formation of Ethylic Cyanotrimethylenecarboxylate, $\begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix}\!\!>\!C(CN)\cdot COOEt$, *and of Ethylic $\alpha\gamma$-Dicyanovalerate,* $CN\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(CN)\cdot COOEt$.

Ethylic Cyanotrimethylenecarboxylate.—The following method has been found to give the best results in the preparation of this compound: 5 grams of sodium are dissolved in 70 grams of absolute alcohol, and when the liquid is quite cold, 25 grams of ethylic cyanacetate are added. After the ethylic sodiocyanacetate has separated, 25 grams of ethylene dibromide are poured in and the mixture carefully heated to boiling on the water-bath in a reflux apparatus. A vigorous reaction sets in, which is sufficient to keep the liquid

boiling for 2—3 minutes. The decomposition is then complete, and a few drops of the liquid, diluted with water, give a neutral reaction with litmus paper.

In order to isolate the product, the alcohol is distilled off and the residue treated with sufficient water to dissolve the sodium bromide. After extracting with ether, washing the ethereal solution with water and dilute potassium carbonate solution (which removes all the red colouring matter), drying over calcium chloride, and distilling off the ether, an almost colourless oil remains, which is next fractionally distilled in steam. The first part of the distillate contains any unchanged ethylene dibromide, and as soon as this ceases to come over, the receiver is changed and the distillation continued so long as oily drops continue to be carried over. This portion of the distillate contains a mixture of ethylic cyanacetate and cyanotrimethylenecarboxylate. A small quantity of a thick oil, which remains in the distillation flask, solidifies on cooling and consists of crude ethylic $\alpha\delta$-dicyanovalerate. The steam distillate is now saturated with ammonium sulphate and extracted with ether, the ethereal solution dried over calcium chloride, the ether distilled off, and the residual oil fractionated 2 or 3 times under ordinary pressure. In this way, ethylic cyanotrimethylenecarboxylate is ultimately obtained as a colourless liquid boiling at 210—211° under 766 mm. pressure.

0·1271 gave 0·2784 CO_2 and 0·0774 H_2O. C = 59·73; H = 6·77.
0·2614 ,, 22·6 c.c. of nitrogen at 18·5° and 770 mm. N = 10·09.
$C_7H_9NO_2$ requires C = 60·41; H = 6·47; N = 10·09 per cent.

Cyanotrimethylenecarboxylic Acid, $\begin{matrix}CH_2\\ |\\ CH_2\end{matrix}\!\!>\!C(CN)\cdot COOH$.

In order to prepare this acid, 3 grams of ethylic cyanotrimethylenecarboxylate, dissolved in 10 c.c. of methylic alcohol, were mixed with a slight excess of cold methyl alcoholic potash containing a little water, when hydrolysis took place very rapidly. The excess of caustic alkali was neutralised with carbon dioxide, and the alcohol then completely removed by evaporation on the water-bath; the residue was dissolved in water, acidified with dilute sulphuric acid, saturated with ammonium sulphate, and extracted 10 times with pure ether. After drying the ethereal solution over anhydrous sodium sulphate, the bulk of the ether was distilled off, and the concentrated solution left to crystallise over sulphuric acid; by this means, the acid was obtained in long, colourless prisms which were nearly pure and melted at 145—147·5°. The crystals were pressed on a porous plate to free them from adherent oily matter,

crystallised from a mixture of ether and light petroleum (b. p. 60—80°), and dried at 100°.

0·2576 gave 0·5142 CO_2 and 0·1119 H_2O. C = 54·43; H = 4·82.
0·1867 „ 21·3 c.c. of nitrogen at 19·5° and 738 mm. N = 12·69.
$C_5H_5NO_2$ requires C = 54·31; H = 4·53; N = 12·64 per cent.

Cyanotrimethylenecarboxylic acid melts at 149°, and, if carefully heated, most of it may be sublimed unchanged. Above 173°, however, it begins to decompose with evolution of carbon dioxide, but no volatile distillate is obtained as in the case of the corresponding cyanotetramethylenecarboxylic acid (p. 932). It is very soluble in water, and the solution reacts strongly acid to litmus paper. Warm ether and benzene dissolve it rapidly, but it is sparingly soluble in light petroleum. The yield of cyanotrimethylenecarboxylic acid, calculated from the ethylic cyanacetate employed in the synthesis, is as much as 50 per cent. of the theoretical. With ferric chloride, a neutral solution of the ammonium salt gives a brown precipitate, which dissolves on gently warming to a clear, red liquid; on boiling, a brown, fluffy precipitate is obtained, which after this cannot be redissolved.

The *silver* salt, $C_5H_4NO_2Ag$, was prepared by dissolving the acid in water and shaking with an excess of freshly-prepared silver carbonate; the whole was then warmed carefully to 50°, and, after cooling, filtered. The liquid cannot be concentrated on the water-bath, as, under these circumstances, the salt undergoes decomposition. The solution was therefore allowed to evaporate in a vacuum at the ordinary temperature, when the silver salt separated in the course of several days in lustrous prisms.

0·1189 gave 0·0588 Ag. Ag = 49·45
0·0884 „ 0·0438 Ag. Ag = 49·43
$C_5H_4NO_2Ag$ requires Ag = 49·52 per cent.

The *barium* salt was prepared by dissolving barium carbonate in an aqueous solution of the acid. It is left as a colourless syrup on evaporating nearly to dryness, but on cooling, this solidifies to a hard cake of prisms which was powdered and dried at 150—160° for analysis.

0·2131 gave 0·1356 $BaSO_4$. Ba = 37·40.
0·2050 „ 0·1307 $BaSO_4$. Ba = 37·50.
$(C_5H_4NO_2)_2Ba + \frac{1}{2}H_2O$ requires Ba = 37·43 per cent.

Amide of Cyanotrimethylenecarboxylic Acid, $\begin{matrix}CH_2\\|\\CH_2\end{matrix}>C(CN)\cdot CO\cdot NH_2$.—In order to prepare this substance, 2 grams of ethylic cyanotrimethylenecarboxylate were shaken with concentrated aqueous

ammonia (sp. gr. 0·88). After 1½ hours the separation of the amide in white, glistening needles had begun, and was complete in about 7 hours. The crystals, which melted at 160°, were collected, dried at 120°, and analysed.

0·1838 gave 41·5 c.c. of nitrogen at 17·5° and 736 mm. N = 25·30.
$C_5H_6N_2O$ requires N = 25·50 per cent.

Attempts to Prepare Cyanotrimethylene.

The following experiments were made with the object of preparing cyanotrimethylene, but were unsuccessful.

(i) 2 grams of cyanotrimethylenecarboxylic acid were distilled from a small retort in a current of carbon dioxide. The substance melted and partly sublimed, and as the temperature was gradually raised above 173°, decomposition set in with much charring, and became very rapid as the temperature approached 200°, but very little or no volatile oil was produced.

(ii) 0·5 gram was heated in a closed tube at 180° with 1 c.c. of water for an hour. On opening the tube, pressure of gas was noticed, and, on examination, this was found to be due in part to carbon dioxide. The brownish-coloured liquid was distilled in steam, but the distillate contained only ammonia. The residue was evaporated on the water-bath and left a brown oil soluble in water with an acid reaction.

(iii) A small quantity of the powdered silver salt was carefully heated; very little charring occurred, and an oil was given off which condensed to a crystalline mass on the cooler parts of the tube.

Conversion of Cyanotrimethylenecarboxylic Acid into Trimethylenedicarboxylic Acid.

The pure cyano-acid was dissolved in concentrated aqueous potash and the solution boiled in a reflux apparatus, when rapid evolution of ammonia was at once noticed, and at the end of 6 hours the liquid was allowed to cool, acidified with dilute sulphuric acid, saturated with ammonium sulphate, and extracted 12 times with pure ether. The ethereal solution was dried over anhydrous sodium sulphate, the bulk of the ether distilled off, and the concentrated solution set aside to crystallise. By this means, trimethylenedicarboxylic acid was obtained in quantity melting at 133—136°, and with this the following characteristic derivatives were prepared.

(i) 3 grams were dissolved in a little concentrated aqueous hydrobromic acid of sp. gr. 1·83, when, on cooling, the whole set to a white, solid cake. This was spread on a porous plate to drain, and purified

by crystallisation from chloroform. In this way, the characteristic crystals of bromethylmalonic acid, melting at 116°, were obtained.

0·2517 gave 0·2250 AgBr. Ag = 38·02.
0·1884 „ 0·1694 AgBr. Ag = 38·27.
$BrCH_2 \cdot CH_2 \cdot CH(COOH)_2$ requires Br = 37·91 per cent.

(ii) 0·7 gram was converted into the acid barium salt, which is recommended by Fittig and Röder for the identification of the acid. The salt crystallised from aqueous solutions in prisms, and had all the properties ascribed to it by these observers.

Ethylic aδ-Dicyanovalerate, $CN \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH(CN) \cdot COOC_2H_5$. The following method of preparation has been found to give the best yield of this compound: 59 grams of ethyl sodiocyanacetate, suspended in 140 grams of alcohol, are heated with 41 grams of ethylene dibromide for 5 hours in a soda-water bottle at 100°. When cool, the contents are transferred to a flask, the alcohol distilled off, and the residue treated with sufficient water to dissolve the sodium bromide. The liquid is extracted with ether, and the ethereal solution washed several times with water and dilute potassium carbonate solution, by which means the deep red colour of the solution may be entirely removed. After drying over calcium chloride and distilling off the ether, a yellowish-green liquid is left, which, on standing in a cool place, gradually deposits the bulk of the ethylic aδ-dicyanovalerate in a crystalline form. The quickest method of isolating the substance consists, however, in distilling the crude product in steam, when ethylic cyanacetate and cyanotrimethylenecarboxylate distil over, leaving an oily residue which solidifies to a mass of prisms. The water is poured off and the crystals, after being freed from oily impurities by washing with a small quantity of alcohol, are crystallised from a mixture of alcohol and light petroleum (b. p. 60—80°). In this way, the substance may be obtained almost colourless, although the crystals usually have a yellowish tinge. The crystals, obtained by setting aside the original, yellowish-green liquid to cool, invariably have a greenish tinge which no amount of recrystallisation will remove. In the form of powder, however, both varieties are white. The sample for analysis was dried at 100°; it then melted at 119·5°, and gave on analysis the following numbers:

0·2364 gave 0·5180 CO_2 and 0·1446 H_2O. C = 59·76; H = 6·79.
0·1800 „ 24·5 c.c. of nitrogen at 17·5° and 766·5 mm. N = 15·89.
0·1580 „ 21·6 „ „ 17·5° „ 752·7 mm. N = 15·67.
$C_9H_{12}N_2O_4$ requires C = 59·97; H = 6·66; N = 15·59 per cent.

When prepared by digesting the sodium compound of ethylic cyanacetate with ethylene dibromide at the ordinary pressure (p. 925), ethylic

$\alpha\delta$-dicyanovalerate was obtained in the form of crystals which melt between 95° and 96°. These crystals were readily obtained in large, colourless, transparent prisms by recrystallisation from a mixture of alcohol and light petroleum (b. p. 60—80°), and had all the appearance of a pure substance. Repeated recrystallisation from this solvent did not raise the melting point above 96°; nevertheless, later investigation has shown that some impurity is not removed by this method. We were led to suspect the identity of this substance with that melting at 119·5° by the circumstance that exactly the same yield of adipic acid (80 per cent.) could be obtained from each. Accordingly, 5 grams of the substance melting at 95—96° were fractionally crystallised from absolute alcohol, when, after the third recrystallisation, the melting point reached 119·5°, and was not raised by further treatment in this manner. A portion thus obtained was mixed with a portion of the substance obtained under pressure; the melting point remained unchanged at 119·5°. In order to set the question of identity at rest, a complete analysis was made.

0·1491 gave 3278 CO_2 and 0·0900 H_2O. C = 59·96; H = 6·70.
0·1715 ,, 22·9 c.c. nitrogen at 19° and 762·5 mm. N = 15·41.
$C_9H_{12}N_2O_4$ requires C = 59·97; H = 6·66; N = 15·59 per cent.

Ethylic $\alpha\delta$-dicyanovalerate is insoluble in cold water and light petroleum, appreciably soluble in boiling water, light petroleum, and cold alcohol, and very soluble in boiling alcohol.

Conversion of Ethylic $\alpha\delta$-Dicyanovalerate into Adipic Acid.

After several failures, the requisite conditions for this transformation were discovered, and a very good yield of adipic acid obtained. Three grams of the cyano-ethereal salt were treated with the calculated quantity of cold methyl alcoholic potash needed to hydrolyse the $COOC_2H_5$ group. The alcohol was then evaporated off, and the residue boiled in a reflux apparatus with concentrated aqueous potash until ammonia ceased to be given off, which is the case in about two hours. Finally, the liquid was mixed with excess of 30 per cent. sulphuric acid, boiled for thirty minutes, and then set aside to crystallise. About 1·5 grams of an acid crystallised out, and another half gram was obtained by saturating the liquid with ammonium sulphate and extracting with ether. The acid, which is nearly colourless, melts at 148·5—149°; it is readily purified by crystallisation from hot water with the aid of animal charcoal, and is thus obtained in the form of colourless, lustrous plates melting at 149—149·5°. The samples for analysis were dried at 120°.

I, Acid obtained from ethylic $\alpha\delta$-dicyanovalerate prepared under pressure.

0·1749 yielded 0·3186 CO_2 and 0·1127 H_2O. C = 49·68; H = 7·09.

II, Acid obtained from ethylic $\alpha\delta$-dicyanovalerate prepared at the ordinary pressure:

0·1716 gave 0·3103 CO_2 and 0·1067 H_2O. C = 49·31; H = 6·90.

$C_6H_{10}O_4$ requires C = 49·31; H = 6·85 per cent.

Specimens of the two acids were crystallised from concentrated nitric acid, and the aqueous solutions, on testing qualitatively, gave the characteristic reactions of adipic acid.

It should be mentioned that several attempts were made to prepare $\alpha\delta$-dicyanovaleric acid from its ethereal salt by hydrolysis with cold methyl alcoholic potash, but without success.

Action of Trimethylene Dibromide on Ethylic Sodiocyanacetate. Formation of Ethylic Cyanotetramethylenecarboxylate, $\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot C(CN)\cdot COOC_2H_5\end{matrix}$.

The method of preparation is exactly analogous to that followed in the case of the corresponding trimethylene compound. The reaction is, however, more vigorous in the present instance, and some care is needed to prevent considerable loss of substance caused by the reacting mixture being thrown out of both flask and reflux condenser. By regulating the temperature carefully and shaking continuously, the reaction may be made to proceed evenly and with no violence. The isolation and purification of the product are conducted exactly as in the case of the trimethylene compound, and the oil boiling at 213—214° under 766 mm. pressure gave the following numbers on analysis:

0·2014 gave 0·4327 CO_2 and 0·1276 H_2O. C = 58·59; H = 7·04.

0·2038 yielded 16·5 c.c. nitrogen at 18·5° and 765 mm. N = 9·39.

$C_8H_{11}NO_2$ requires C = 62·72; H = 7·19; N = 9·14 per cent.

The analytical numbers show that the liquid is not pure ethylic cyanotetramethylene carboxylate, but still contains ethylic cyanacetate.

Cyanotetramethylenecarboxylic Acid, $\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot C(CN)\cdot COOH\end{matrix}$.

The method of preparation differs in no respect from that of the corresponding trimethylene compound. The acid, which melts at 69—70°, is left as an oil by the evaporation of its concentrated ethereal solution, and only solidifies to a mass of colourless prisms after some

time. These are dried on a porous plate and recrystallised from pure carbon bisulphide containing a few drops of ether. In this way, magnificent, long, silky needles are obtained.

0·2540 gave 0·5343 CO_2 and 0·1366 H_2O. C = 57·37; H = 5·97.
0·2090 „ 20·5 c.c. nitrogen at 17° and 748 mm. N = 11·20.
$C_6H_7NO_2$ requires C = 57·58; H = 5·59; N = 11·22 per cent.

Cyanotetramethylenecarboxylic acid may be sublimed unchanged if a small quantity be heated just above its melting point for some time, but the temperature must not be allowed to reach 160°, as at this point decomposition into cyanotetramethylene and carbon dioxide takes place. It is soluble in water, ether, chloroform, benzene, and acetone at the ordinary temperature, and in warm, but not in cold, carbon disulphide. A neutral solution of the ammonium salt in water, when treated with aqueous ferric chloride, behaves in a similar manner to that already described in the case of the corresponding trimethylene compound. The silver and barium salts of cyanotetramethylenecarboxylic acid were prepared in the same way as, and exhibit complete analogy to, the salts of the corresponding trimethylene acid.

Analysis of *silver* salt.

0·1106 gave 0·0516 Ag. Ag = 46·65.
0·1787 „ 0·0839 Ag. Ag = 46·95.
$C_6H_6NO_2Ag$ requires Ag = 46·53 per cent.

Analysis of the *barium* salt (dried at 140°).

0·1964 gave 0·1168 $BaSO_4$. Ba = 34·93.
0·2282 „ 0·1349 $BaSO_4$. Ba = 34·75.
$(C_6H_6NO_2)_2Ba + \frac{1}{2}H_2O$ requires Ba = 34·77 per cent.

Conversion of Cyanotetramethylenecarboxylic Acid into Tetramethylenedicarboxylic Acid.

This change is most readily effected by means of boiling concentrated aqueous potash, and the method of procedure is exactly the same as that described in detail in the case of the corresponding trimethylene derivative. In this way, an acid was obtained crystallising in colourless prisms which melted at 157°, and showed all the characteristic properties of tetramethylenedicarboxylic acid (m. p. 156°); it was dried at 120°, and was analysed with the following results:

0·1721 gave 0·3188 CO_2 and 0·0883 H_2O. C = 50·52; H = 5·70.
$C_6H_8O_4$ requires C = 50·00; H = 5·55 per cent.

The characteristic lead salt was prepared and analysed, after being dried in the air for 3 days.

0·2548 yielded 0·2107 $PbSO_4$. Pb = 56·43.
0·2745 lost 0·014 H_2O at 140°. H_2O = 5·10.
$C_6H_6O_4Pb + H_2O$ requires Pb = 56·33; H_2O = 4·91 per cent.

After being dried in a vacuum for 3 days,

0·4035 yielded 0·3507 $PbSO_4$. Pb = 59·33.
0·2846 ,, 0·2460 $PbSO_4$. Pb = 59·00.
$C_6H_6O_4Pb$ requires Pb = 59·24 per cent.

There is a slight discrepancy between these results and those given in the earlier description of this salt (Perkin, Trans., 1887, **51**, 8). It is there stated that the salt dried in a vacuum still contains $1H_2O$, but this is not the case, as is shown by the fact that a specimen of the lead salt prepared from tetramethylenedicarboxylic acid, obtained with the aid of ethylic malonate, after drying for 3 days in a vacuum, gave the following result on analysis:

0·2438 gave 0·2121 $PbSO_4$. Pb = 59·35.
$PbC_6H_6O_4$ requires Pb = 59·24 per cent.

As the salts made from the two specimens of the acid resemble one another in every respect, and especially in their characteristic property of passing from the amorphous to the crystalline state on standing for a short time, or more quickly still on shaking, no doubt can exist as to their identity. Each salt, when dried in the air, contains $1H_2O$, but this is given up, either on heating to 140° or on standing in a vacuum.

Cyanotetramethylene, $\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CH\cdot CN\end{matrix}$.

In order to prepare this interesting substance, 12 grams of cyanotetramethylenecarboxylic acid were distilled in portions of 6 grams at a time from a small retort heated in a bath of fusible metal. Carbon dioxide is given off very readily from 160° upwards, and the whole of the liquid (7·8 grams) distilled over below 190°. On redistilling the oil, it was found that the carbon dioxide had not been completely split off in one distillation, but after two more fractionations, about 5—5·5 grams of a liquid were obtained, boiling constantly at 148—149° under 760 mm. pressure.

0·1980 gave 0·5344 CO_2 and 0·1591 H_2O. C = 73·60; H = 8·92.
0·2301 ,, 34·6 c.c. nitrogen at 19·5° and 753·5 mm. N = 17·09.
C_5H_7N requires C = 74·03; H = 8·64; N = 17·32 per cent.

The yield of cyanotetramethylene obtained by this reaction is at least 70 per cent. of the theoretical; it is a colourless, very mobile liquid,

has a pleasant odour, and is hydrolysed almost quantitatively by boiling concentrated aqueous potash to the corresponding tetramethylene-monocarboxylic acid, $\begin{matrix}CH_2\cdot CH_2\\ |\quad\ |\\ CH_2\cdot CH\cdot COOH\end{matrix}$.

4·3 grams of cyanotetramethylene were boiled with 6 grams of potash dissolved in 20 c.c. of water for 6—7 hours in a reflux apparatus. When the evolution of ammonia had ceased, the liquid was allowed to cool, and then acidified with dilute sulphuric acid; the colourless oil which separated was extracted with ether in the usual way, and, after drying over anhydrous sodium sulphate and distilling off the ether, the residual liquid, on fractionation, passed over between 190° and 193°. This was again distilled, and the fraction 191—192° analysed.

0·2842 gave 0·6234 CO_2 and 0·2060 H_2O. C = 59·82; H = 8·05.
$C_5H_8O_2$ requires C = 60·00; H = 8·00 per cent.

The characteristic calcium salt of this acid was prepared; it is very soluble in water, and crystallises from very concentrated solutions in silky needles.

Preparation of Pimelic Acid from the Bye-product of the Reaction between Trimethylene Dibromide and Ethylic Sodiocyanacetate.

The thick oil, which is left in the steam distillation flask, after distilling off the ethylic cyanacetate and cyanotetramethylenecarboxylate, and does not solidify on cooling, probably consists of diethylic $\alpha\alpha_1$-dicyanopimelate,

$$COOC_2H_5\cdot CH(CN)\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(CN)\cdot COOC_2H_5.$$

It was extracted with ether, the ethereal solution dried over calcium chloride, and the ether distilled off; the residual oil was then boiled for about 20 hours in a reflux apparatus with concentrated aqueous potash. At the end of this time, complete hydrolysis had taken place, and the evolution of ammonia ceased. The liquid was acidified with sulphuric acid, and, after saturating with ammonium sulphate, extracted with ether; the ethereal solution was dried over anhydrous sodium sulphate and the ether distilled off, when an oil was left which was heated in a bath of fusible metal to 210° until the evolution of carbon dioxide had ceased. The dark coloured residue, which showed no signs of crystallising, was etherified by heating with 5 times its volume of absolute alcohol and one-fifth its volume of concentrated sulphuric acid for 2 hours in a reflux apparatus. The product was poured into water, extracted with ether, washed with sodium carbonate solution, dried, and the ether distilled off. On fractionating the residue at 40 mm. pressure, almost the

whole quantity distilled between 160° and 180°. This fraction was hydrolysed by boiling with methyl alcoholic potash, and after complete removal of the alcohol by evaporation with water, the residue was acidified and extracted with ether in the usual way. On allowing the ethereal solution to evaporate in a vacuum, an acid crystallised out which melted between 97° and 102°, and after recrystallising from benzene was finally obtained in a pure condition; it melted at 105°, and consisted of pure pimelic acid, as the following analysis shows:

0·1429 gave 0·2775 CO_2 and 0·1004 H_2O. C = 52·33; H = 7·80.
$C_7H_{12}O_4$ requires C = 52·50; H = 7·50 per cent.

This acid gave a calcium salt, which separated from its cold, saturated solution on heating, a behaviour which is also shown by the calcium salt of normal pimelic acid.

The authors wish to reserve the further examination of the substances described in this paper.

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RICHARD CLAY AND SONS, LIMITED, LONDON AND BUNGAY.

β-ALDEHYDOPROPIONIC ACID, $CHO{\cdot}CH_2{\cdot}CH_2{\cdot}COOH$, AND β-ALDEHYDOISOBUTYRIC ACID, $CHO{\cdot}CH_2{\cdot}CH(CH_3){\cdot}COOH$.

BY

WILLIAM H. PERKIN, JUN.,

AND

CHARLES H. G. SPRANKLING.

From the Transactions of the Chemical Society, 1899.

β-Aldehydopropionic Acid, $CHO\cdot CH_2\cdot CH_2\cdot COOH$, and β-Aldehydoisobutyric Acid, $CHO\cdot CH_2\cdot CH(CH_3)\cdot COOH$.

By W. H. Perkin, jun., and C. H. G. Sprankling.

Some time since (Trans., 1896, 69, 162), a paper was published by one of us in conjunction with Messrs. W. H. Bentley and E. Haworth which had for one of its objects the discovery of a method for introducing the group $\cdot CH_2\cdot CH_2\cdot OH$ into organic substances, a synthetical process which, if it could be easily carried out, would be very valuable as a means of forming ring compounds. It was found that the action of glycol chlorhydrin, $Cl\cdot CH_2\cdot CH_2\cdot OH$, on the sodium compounds of substances like ethylic acetoacetate, ethylic malonate, and their derivatives, did not, except in isolated cases, yield the desired result; ultimately, however, a method was devised which in the few cases tried gave fairly satisfactory results, and which may be briefly stated in the form of an example thus.

β-Bromethyl phenyl ether, $C_6H_5\cdot O\cdot CH_2\cdot CH_2Br$, was prepared by acting on sodium phenoxide with ethylene bromide, and this, when digested with the sodium derivative of ethylic methylmalonate, yielded ethylic γ-phenoxyethylmethylmalonate,

$$C_6H_5\cdot O\cdot CH_2\cdot CH_2\cdot C(CH_3)(COOC_2H_5)_2.$$

The acid corresponding to this ethereal salt, when heated at 100°, loses

one molecule of carbon dioxide with formation of γ-phenoxyethylmethylacetic acid, $C_6H_5\cdot O\cdot CH_2\cdot CH_2\cdot CH(CH_3)\cdot COOH$, from which hydrobromic acid eliminates the phenyl group and forms γ-bromethylmethylacetic acid, $CH_2Br\cdot CH_2\cdot CH(CH_3)\cdot COOH$. This brom-acid when boiled with sodium carbonate, gives the sodium salt of hydroxyethylmethylacetic acid, $OH\cdot CH_2\cdot CH_2\cdot CH(CH_3)\cdot COONa$, from which, on acidifying, methylbutyrolactone $\begin{matrix}CH_2\cdot CH_2\cdot CH\cdot CH_3\\ |\quad\quad\quad\quad |\\ O\text{——}\quad\quad\text{——}CO\end{matrix}$, is at once obtained. When this method was tried in more complicated synthetical experiments, it did not work well, partly owing to the number of operations involved, but principally on account of the smallness of the yield obtained in some of these operations. For these reasons, experiments were made with a view to discover a more direct method, and ultimately we found in *bromacetal*, $(C_2H_5O)_2CH\cdot CH_2Br$, a substance which seems likely to answer the purpose.

Bromacetal reacts readily with the sodium derivative of ethylic malonate, yielding *ethylic acetalmalonate* according to the equation

$$(C_2H_5O)_2CH\cdot CH_2Br + CHNa(COOC_2H_5)_2 = (C_2H_5O)_2CH\cdot CH_2\cdot CH(COOC_2H_5)_2 + NaBr.$$

This ethylic salt, which distils without decomposition at 151—154° (15 mm.), yields, on hydrolysis, the corresponding *acetalmalonic acid*, $(C_2H_5O)_2CH\cdot CH_2\cdot CH(COOH)_2$, and this, when heated with water at 180° is decomposed into alcohol, carbon dioxide, and *β-aldehydopropionic acid*, $(C_2H_5O)_2CH\cdot CH_2\cdot CH(COOH)_2 + H_2O = CHO\cdot CH_2\cdot CH_2\cdot COOH + 2C_2H_5\cdot OH + CO_2$. β-Aldehydopropionic acid is a new and very interesting substance, since it is the "half-aldehyde" of succinic acid and belongs to the class of aldehyde acids of which, so far, very few have been prepared. Its properties show that it is a true aldehyde, and not a hydroxymethylene compound of the formula

$$CH(OH):CH\cdot CH_2\cdot COOH,$$

it therefore, does not belong to the class of substances which Claisen has investigated with such brilliant results. Aldehydopropionic acid is an almost colourless liquid which reduces Fehling's solution and gives a violet coloration with a solution of rosaniline hydrochloride decolorised by sulphurous acid. It is slowly oxidised in contact with air, rapidly by nitric acid, with formation of succinic acid, and when reduced with sodium amalgam it yields *butyrolactone*,

$$CHO\cdot CH_2\cdot CH_2\cdot COOH = OH\cdot CH_2\cdot CH_2\cdot CH_2\cdot COOH = \begin{matrix}CH_2\cdot CH_2\cdot CH_2\\ |\quad\quad\quad\quad |\\ O\text{——}\quad\quad\text{——}CO\end{matrix}.$$

When boiled with caustic soda solution in a flat basin, aldehydopropionic acid undergoes a most interesting change, yielding small quantities of *terephthalic acid*, the dihydroterephthalic acid, which may be assumed to be the first product of the condensation, being oxidised to tere-

phthalic acid by the action of the air,

$$\begin{array}{rcl} \mathrm{CHO{\cdot}CH_2{\cdot}CH_2{\cdot}COOH} & & \mathrm{CH{\cdot}CH_2{\cdot}C{\cdot}COOH} \\ \mathrm{COOH{\cdot}CH_2{\cdot}CH_2{\cdot}CHO} & = & \mathrm{COOH{\cdot}C\cdot CH_2\cdot CH} \\ & & \mathrm{CH{\cdot}CH{:}C{\cdot}COOH} \\ & = & \mathrm{COOH{\cdot}C\cdot CH{:}CH} \end{array}$$

and this is, so far, the only experiment which has been instituted with the object of testing the value of aldehydopropionic acid in condensation experiments.

The action of bromacetal on sodium compounds is probably a general one, since we have found that the reaction proceeds equally well when the sodium derivative of ethylic methylmalonate is substituted for that of ethylic malonate in the above experiments.

The *ethylic acetalmethylmalonate*,

$$(C_2H_5O)_2CH{\cdot}CH_2{\cdot}C(CH_3)(COOC_2H_5)_2,$$

thus obtained yields *acetalmethylmalonic* acid,

$$(C_2H_5O)_2{\cdot}CH{\cdot}CH_2{\cdot}C(CH_3)(COOH)_2,$$

on hydrolysis, and this, when heated with water at 180°, is converted into β-aldehydoisobutyric acid, $CHO{\cdot}CH_2{\cdot}CH(CH_3){\cdot}COOH$, a liquid acid which, on oxidation, yields methyl succinic acid,

$$COOH{\cdot}CH_2{\cdot}CH(CH_3){\cdot}COOH.$$

Further experiments on the action of bromacetal on the sodium compounds of ethereal salts are in progress. It should be mentioned, in conclusion, that C. Harries (*Ber.*, 1898, **31**, 42) obtained a substance which is probably the methylal of the half-aldehyde of succinic acid, $(CH_3O)_2CH{\cdot}CH_2{\cdot}CH_2{\cdot}COOH$, by the action of sodium hypobromite on levulin methylal, $(CH_3O)_2CH{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}CH_3$, but he does not appear to have further investigated this substance.

Action of Bromacetal on the Sodium Derivative of Ethylic malonate. Formation of Ethylic Acetalmalonate, $(C_2H_5O)_2CH{\cdot}CH_2{\cdot}CH(COOC_2H_5)_2$.

Ethylic acetalmalonate is conveniently prepared as follows. Sodium (14·2 grams) is dissolved in absolute alcohol (170 grams) and the solution, while still warm, is mixed with ethylic malonate (100 grams) and bromacetal (80 grams) and the mixture, inclosed in sealed tubes, is heated at 130—140° for 4 hours; when as much alcohol as possible has been removed from the product by distillation on the water bath, water is added to the residue and the precipitated oil extracted several times with ether. The ethereal solution is washed, well dried over calcium chloride, the ether distilled off, and the residual oil fractionated under reduced pressure (15 mm.). More than half passes over below 145° and consists of a mixture of unchanged ethylic malonate and bromacetal, whilst the fraction distilling between 145° and 165°

contains the ethylic acetalmalonate. The oil boiling below 145° (15 mm.), and which was assumed to contain about 50 per cent. of bromacetal, was again heated in sealed tubes with the calculated quantity of the sodium derivative of ethylic malonate, the temperature, however, being now allowed to rise to 160°.

In this way, practically the whole of the bromacetal was converted into crude ethylic acetalmalonate boiling at 145—165° (15 mm.), and from this fraction the almost pure ethereal salt could be obtained by repeated fractionation as a colourless oil of a peculiar and not unpleasant odour, and boiling at 151—154° (15 mm.), or at 166—168° (at 26 mm.). Analysis.*

0·1821 gave 0·3714 CO_2 and 0·1418 H_2O. C = 55·62; H = 8·65.
0·1640 „ 0·3360 CO_2 „ 0·1282 H_2O. C = 55·87; H = 8·67.
$(C_2H_5O)_2CH{\cdot}CH_2{\cdot}CH(COOC_2H_5)_2$ requires C = 56·50; H = 8·69 per cent.

Acetalmalonic Acid, $(C_2H_5O)_2CH{\cdot}CH_2{\cdot}CH(COOH)_2$.

Acetalmalonic acid is obtained by hydrolysing its ethereal salt with alcoholic potash, but the operation has to be carefully performed, since prolonged boiling with the alkali decomposes the acid with elimination of the group $\cdot CH_2{\cdot}CH(OC_2H_5)$, and formation of malonic acid. It is not clear how this decomposition takes place, but there can be no doubt as to the formation of malonic acid, since, in one instance, when a quantity of this acid was obtained melting at 131°, an analysis was carried out with the following results.

0·2687 gave 0·3480 CO_2 and 0·0972 H_2O. C = 35·32; H = 4·26.
$CH_2(COOH)_2$ requires C = 34·63; H = 3·86 per cent.

It was very soluble in water, and when heated decomposed with evolution of carbon dioxide and formation of acetic acid.

If, however, the action of the potash is only allowed to proceed for a short time, hydrolysis takes place normally, and a good yield of acetalmalonic acid is obtained. After many experiments, we found that the following process gave the best results. Ten grams of the pure ethereal salt is mixed with a solution of 6 grams of pure potash in alcohol, and the mixture heated on the water-bath for 10 minutes, the alcohol is then rapidly driven off on the water-bath and the cold residue mixed with an excess of dilute sulphuric acid and extracted repeatedly with ether. The ethereal solution, after drying and evaporating, deposits a thick oil which shows no sign of crystallising, even after standing for some days over sulphuric acid in a vacuum. On

* The numbers obtained are slightly low, on account of the oil containing traces of bromine, which it was found impossible to remove by fractionation.

analysis,* it gave numbers agreeing approximately with those required for acetalmalonic acid.

I. 0·1150 gave 0·2040 CO_2 and 0·0722 H_2O. C = 49·15 ; H = 6·97.
II. 0·1779 „ 0·3177 CO_2 „ 0·1200 H_2O. C = 48·72 ; H = 7·47.
III. 0·1974 „ 0·3529 CO_2 „ 0·1227 H_2O. C = 48·75 ; H = 6·91.
IV. 0·1537 „ 0·2719 CO_2 „ 0·0915 H_2O. C = 48·26 ; H = 6·61.
$(COOH)_2CH\cdot CH_2\cdot CH(OC_2H_5)_2$ requires C = 49·05 ; H = 7·27 per cent.

Silver salt.—Acetalmalonic acid is very soluble in water, and if the aqueous solution is neutralised with ammonia, and silver nitrate added, a dense, white precipitate of the silver salt is precipitated, which, after washing first with water and then with alcohol and ether, gave the following results on analysis.

0·2177 gave, on ignition, 0·1092 Ag. Ag = 50·16.
$(C_2H_5O)_2CH\cdot CH_2\cdot CH(COOAg)_2$ requires Ag = 49·79 per cent.

Distillation of Acetalmalonic Acid.—When this acid is heated in a fractionating flask, decomposition soon sets in with evolution of carbon dioxide, and the residue, after repeatedly fractionating under reduced pressure, yields a liquid which boils, apparently constantly, at 157—161° (15 mm.), and which was at first thought to be acetalacetic acid $(C_2H_5O)_2CH\cdot CH_2\cdot CH_2\cdot COOH$. The analyses, however, show that this substance consists, for the most part, of aldehydopropionic acid (p. 16), elimination of alcohol having taken place during the distillation owing, probably, to the unavoidable presence of small quantities of water.

0·2658 gave 0·4740 CO_2 and 0·1607 H_2O. C = 48·63 ; H = 6·71.
0·2514 „ 0·4372 CO_2 „ 0·1437 H_2O. C = 48·53 ; H = 6·39.
$COOH\cdot CH_2\cdot CH_2\cdot CHO$ requires C = 47·05 ; H = 5·88 per cent.
$COOH\cdot CH_2\cdot CH_2\cdot CH(OC_2H_5)_2$ requires C = 54·54 ; H = 9·09 per cent.

In order to confirm this view, the liquid was heated with an equal quantity of phenylhydrazine for 10 minutes at 150° and poured into ether, when, on standing, a white, crystalline substance separated, which, after crystallisation from acetic acid, melted at 191° and gave the following results on analysis.

0·0601 gave 0·1502 CO_2 and 0·0350 H_2O. C = 68·17 ; H = 6·47.
0·1258 gave 21·3 c.c. nitrogen at 19° and 768 mm. N = 19·42.
$C_{16}H_{18}N_4O$ requires C = 68·09 ; H = 6·38 ; N = 19·85 per cent.

This substance, on examination, was found to be identical with the condensation product formed by heating aldehydopropionic acid with

* The four analyses given here were carried out with four different preparations of the acid.

phenylhydrazine (see below), and thus it is probable that this aldehydo-acid was present in the oil obtained by the distillation of acetalmalonic acid.

β-Aldehydopropionic acid, $CHO \cdot CH_2 \cdot CH_2 \cdot COOH$.

In order to prepare this substance, acetalmalonic acid is heated with about four times its weight of water at 180—190° for 4 hours, the solution evaporated on the water-bath, and the residue allowed to stand over sulphuric acid in a well exhausted desiccator for 4 or 5 days.

The yellow, oily residue thus obtained, on analysis, gave numbers agreeing approximately with those required for β-aldehydopropionic acid.*

I. 0·2084 gave 0·3611 CO_2 and 0·1127 H_2O. C = 47·40; H = 6·01.
II. 0·2124 „ 0·3675 CO_2 „ 0·1132 H_2O. C = 47·20; H = 5·92.
III. 0·1703 „ 0·2928 CO_2 „ 0·0890 H_2O. C = 46·89; H = 5·82.
IV. 0·1379 „ 0·2300 CO_2 „ 0·0806 H_2O. C = 45·47; H = 6·47.
V. 0·1576 „ 0·2649 CO_2 „ 0·0909 H_2O. C = 45·90; H = 6·40.
$CHO \cdot CH_2 \cdot CH_2 \cdot COOH$ requires C = 47·05; H = 5·88 per cent.

β-Aldehydopropionic acid is a slightly brownish liquid which dissolves readily in water, freshly prepared, its solution reduces Fehling's solution, and produces a pink colour when mixed with a solution of rosaniline hydrochloride which has been decolorised with sulphur dioxide. When heated at 150° with phenylhydrazine for 10 minutes, condensation readily takes place, and if the product is poured into ether a white, crystalline substance separates on standing, which, after recrystallisation from acetic acid, gave the following results on analysis.

0·0590 gave 10·1 c.c. nitrogen at 18° and 758 mm. N = 20·00.

This substance, of which a full analysis is given on p. 15, melts at 192° and is evidently the phenylhydrazide of the phenylhydrazone of aldehydopropionic acid, $C_6H_5 \cdot NH \cdot N{:}CH \cdot CH_2 \cdot CH_2 \cdot CO \cdot NH \cdot NH \cdot C_6H_5$, which contains 19·85 per cent. of nitrogen.

Oxidation of Aldehydopropionic Acid. Formation of Succinic Acid.

When aldehydopropionic acid is left exposed to the air, it darkens in colour and gradually deposits crystals, ultimately being converted into a brown, pasty mass, which in contact with porous porcelain slowly

* As this substance would not crystallise, analyses of each preparation were made, and some of these varied as much as 3 per cent. from the theoretical; we therefore wish it to be distinctly understood that we do not consider that the aldehydo-acid made in this way is pure. All the preparations contained a small amount of ash derived from the tube in which they were prepared; this was allowed for in the analyses.

becomes a nearly colourless, crystalline mass, the sticky, oily impurity being only very gradually absorbed.

The crystals were purified by recrystallisation from hydrochloric acid with the aid of animal charcoal, and in this way colourless plates were obtained which melted at 181° and had all the properties of succinic acid. Analysis.

0·1201 gave 0·1786 CO_2 and 0·0561 H_2O. C = 40·56; H = 5·18.
$COOH{\cdot}CH_2{\cdot}CH_2{\cdot}COOH$ requires C = 40·68; H = 5·08 per cent.

This experiment shows that aldehydopropionic acid is slowly converted into succinic acid by the oxygen of the air, and this change takes place very rapidly when oxidising agents are employed. A small quantity of the aldehydo-acid, after being heated to boiling with dilute nitric acid (20 per cent.) for some hours until no further oxidation took place, was evaporated repeatedly on the water-bath with the addition of small quantities of water, until a colourless, crystalline residue was left. This, after recrystallisation from hydrochloric acid, melted at 181—184° and consisted of succinic acid.

0·0598 gave 0·0898 CO_2 and 0·0279 H_2O. C = 40·96; H = 5·18.
$COOH{\cdot}CH_2{\cdot}CH_2{\cdot}COOH$ requires C = 40·68; H = 5·08 per cent.

Reduction of Aldehydopropionic Acid. Formation of Butyrolactone,

Five grams of the pure aldehydo-acid were dissolved in water and treated with three times the calculated quantity of 4 per cent. sodium amalgam, carbon dioxide being passed through the liquid and the temperature kept below 10° during the whole operation, in order to avoid, as far as possible, risk of polymerisation or condensation; after separating the mercury, the solution was made strongly acid with sulphuric acid, heated to boiling for half an hour in a reflux apparatus, and then repeatedly extracted with ether. The ethereal solution, when dried and evaporated, deposited a colourless oil, which, after twice fractionating, boiled at 203—208°. On analysis, it gave numbers agreeing with those of butyrolactone, which, according to Fittig and Roeder (*Annalen*, 227, 1885, 22), boils at 206°.

0·1356 gave 0·2760 CO_2 and 0·0888 H_2O. C = 55·51; H = 7·27.
$C_4H_6O_2$ requires C = 55·81; H = 6·97 per cent.

Action of Caustic Soda on β-Aldehydopropionic Acid. Synthesis of Terephthalic Acid.

This synthesis, which is explained in the introduction to this paper, was carried out as follows. β-Aldehydopropionic acid (10 grams) was dissolved in an excess of dilute sodium hydroxide and the solution evaporated in a flat glass basin nearly to dryness, water was then added and the solution again evaporated, this operation being continued during three days; the concentrated liquid, after being acidified and allowed to stand over-night, deposited a small quantity of a brownish powder, which, on examination, was found to be crude terephthalic acid. This was purified by dissolving it in dilute sodium carbonate, boiling with animal charcoal until most of the colour had been removed, and then treating the solution at 0° with permanganate until the violet colour remained permanent for 2 minutes; the filtrate from the manganese precipitate was concentrated, and, while still hot, acidified with hydrochloric acid; the colourless, crystalline precipitate, which separated rapidly, had all the properties of terephthalic acid. It was almost insoluble in water and ether, did not melt at 270°, and on heating in a small test tube it sublimed apparently without melting.

The small quantity of acid remaining (about 0·2 gram) was converted into its methylic salt by Baeyer's (*Annalen*, 1888, **245**, 140) method by heating with phosphorus pentachloride, mixing the product with methylic alcohol, and purifying the crystals which separated, by recrystallisation from methylic alcohol, with the aid of animal charcoal; the colourless plates thus obtained were very sparingly soluble in methylic alcohol and melted sharply at 140°, the melting point of the methylic salt of terephthalic acid. A specimen of the methylic salt prepared from pure terephthalic acid was found to be identical with the synthetical substance in every respect, moreover, an intimate mixture of the two preparations melted sharply at 140°. These experiments prove conclusively that the acid formed by the action of sodium hydroxide on β-aldehydopropionic acid is terephthalic acid, and it is unfortunate that, in spite of a number of experiments, we have been unable to devise a better method for the condensation of the aldehyde, as the yield of terephthalic acid obtained was certainly not more than 5 per cent.

β-Aldehydoisobutyric Acid, $CHO{\cdot}CH_2{\cdot}CH(CH_3){\cdot}COOH$.

The first step in synthesising this substance was to prepare ethylic acetalmethylmalonate, and this was readily accomplished by heating the sodium derivative of ethylic methylmalonate with bromacetal

under the conditions already described in the case of ethylic acetalmalonate. The ethylic malonate employed in these experiments was made by the etherification of pure methylmalonic acid; the quantities of the substances used in the synthesis of ethylic acetalmethylmalonate were,

Ethylic methylmalonate	54 grams.
Sodium.....	7·2 „
Bromacetal	40 „

After isolating the product in the way described in the case of ethylic acetalmalonate, the crude oil was submitted to careful fractionation and the fraction 165° (26 mm.), which consisted of nearly pure ethylic acetalmethylmalonate, was analysed with the following result.

0·1491 gave 0·3056 CO_2 and 0·1204 H_2O. C = 57·20; H = 8·97.
$(C_2H_5O)_2CH{\cdot}CH_2{\cdot}CH(CH_3)(COOC_2H_5)_2$ requires C = 57·92; H = 8·96 per cent.

Acetalmethylmalonic Acid, $(C_2H_5O)_2{\cdot}CH{\cdot}CH_2{\cdot}CH(CH_3)(COOH)_2$.

This acid, which was prepared by the careful hydrolysis of its ethereal salt, is a colourless syrup readily soluble in water.

0·1965 gave 0·3624 CO_2 and 0·1404 H_2O. C = 50·30; H = 7·94.
$C_{10}H_{18}O_6$ requires C = 51·28; H = 7·69 per cent.

The *silver salt*, prepared by precipitating a neutral solution of the ammonium salt with silver nitrate, is a white, amorphous powder, which readily darkens when exposed to light.

0·2026 gave, on ignition, 0·0980 Ag. Ag = 48·37.
$C_{10}H_{16}Ag_2O_6$ requires Ag = 48·19 per cent.

Aldehydoisobutyric acid, obtained by heating acetalmethylmalonic acid with water at 180° for 4 hours, and evaporating the liquid on a water bath, is an oil which, after standing for some days over sulphuric acid in a vacuum, was analysed with the following results.*

0·1933 gave 0·3653 CO_2 and 0·1238 H_2O. C = 51·53; H = 7·28.
$CHO{\cdot}CH_2{\cdot}CH(CH_3){\cdot}COOH$ requires C = 51·72; H = 6·89 per cent.

This substance is very similar to aldehydopropionic acid in its properties, and its constitution is proved by the fact that, when oxidised with nitric acid, it yields *methylsuccinic* acid; this, after recrystallisation, melted at 110—112°, and gave the correct numbers on analysis.

0·2142 gave 0·3558 CO_2 and 0·1238 H_2O. C = 45·30; H = 6·40.
$COOH{\cdot}CH(CH_3){\cdot}CH_2{\cdot}COOH$ requires C = 45·45; H = 6·06 per cent.

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* See footnote, p. 16.

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THE SYNTHETICAL FORMATION OF BRIDGED RINGS. PART I. SOME DERIVATIVES OF DICYCLOPENTANE.

BY

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J. F. THORPE,

AND

C. WALKER.

From the Transactions of the Chemical Society, 1901. Vol. 79.

LXXXIII.—*The Synthetical Formation of Bridged Rings. Part I. Some Derivatives of Dicyclopentane.*

By W. H. Perkin, jun., and J. F. Thorpe.

A short time ago (Trans., 1899, 75, 48) we showed that ethyl bromodimethylglutarate, when digested with alcoholic potash, yields the potassium salt of *caronic acid*,

$$CO_2Et\cdot CHBr\cdot CMe_2\cdot CH_2\cdot CO_2Et + 4KOH = CO_2K\cdot \underset{\diagup\ \diagdown}{CMe_2}\ CH\cdot CH\cdot CO_2K + 2KBr + 2EtOH + 2H_2O,$$

and this synthesis not only proves the constitution assigned to caronic acid by Baeyer and Ipatieff (*Ber.*, 1892, 29, 2796), but, indirectly, affords strong evidence that the formula of carone,

$$Me\cdot CH\!-\!CO\!-\!CH \begin{matrix} \\ CH_2\cdot CH_2\cdot CH \end{matrix} > CMe_2,$$

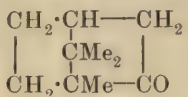
first suggested by Wagner (*J. Russ. Phys. Chem. Soc.*, 1896, 28, 95) is correct. The saturated hydrocarbon,

$$CH_2\cdot CH_2\cdot CH \begin{matrix} \\ CH_2\cdot CH_2\cdot CH \end{matrix} > CH_2,$$

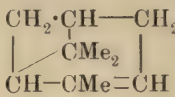
from which carone is derived, is therefore a heptamethylene ring in which two carbon atoms are united to form a trimethylene ring, or, in other words, it is made up of a hexamethylene and a trimethylene ring.

During the last few years, it has frequently been suggested that the constitutions of some members of the terpene and camphor series should be expressed by formulæ containing somewhat similar bridged

or double rings. Thus, for example, camphor and pinene should, according to Bredt, be represented thus:



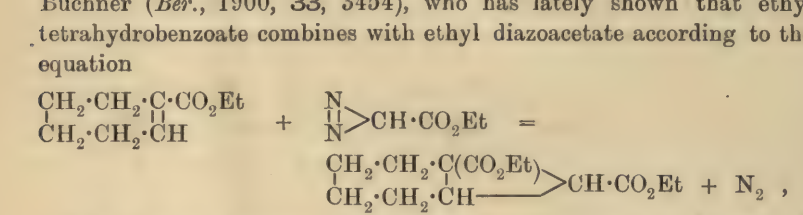
Camphor



Pinene.

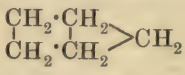
The camphor formula contains two five-carbon rings, the pinene formula, on the other hand, a six- and a four-carbon ring. As it is probable that compounds of this and other similar types will, in the near future, be of common occurrence, it seemed to us that it was a matter of importance to endeavour to discover synthetical methods for the formation of such double or *bridged* rings.

The only work which has been done in this direction is that of Buchner (*Ber.*, 1900, **33**, 3454), who has lately shown that ethyl tetrahydrobenzoate combines with ethyl diazoacetate according to the equation



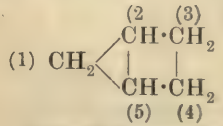
and the product, which he terms ethyl 1 : 2-norcarandicarboxylate, on account of its close relationship to carone, contains a *bridged* heptamethylene ring.

In the present paper, abstracts of which have already appeared (Proc., 1900, **16**, 149; 1901, **17**, 110), we describe the synthesis of a series of compounds derived from the hydrocarbon

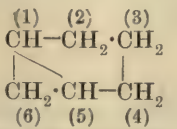


which consists of a pentamethylene ring so bridged as to form a four- and a three-carbon ring united together by two carbon atoms of each.

In endeavouring to devise a general system of nomenclature for bridged rings of this description, we met with very considerable difficulty. Our first suggestion was that the letters γεψ (from γεψυρα, a bridge) should be prefixed to the hydrocarbon, with numbers to indicate the carbon atoms which were united to form the bridge thus:—



2 : 5-γεψ-Pentamethylene.



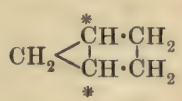
1 : 5-γεψ-Hexamethylene.

but this method cannot be well adapted to substances such as camphor and pinene (p. 730), in which the bridge itself consists of one or more carbon atoms.

In a letter to Professor von Baeyer, one of us mentioned this difficulty, and as the result of a good deal of correspondence, he was good enough to elaborate a scheme for the nomenclature of bridged rings which seems to be of general application, and was subsequently published (*Ber.*, 1901, **33**, 3771). Briefly stated, this scheme is as follows.

Every bridged (or dicyclic) hydrocarbon contains, of necessity, two tertiary carbon atoms which are either directly united to form the bridge, or else indirectly united when the bridge is itself made up of carbon atoms: in the first place, the bridge is called 0, in the second case 1, 2, &c., according to the number of carbon atoms which it contains.

Furthermore, every dicyclic hydrocarbon, contains three bridges as will be clearly seen from the study of the case of *dicyclopentane*,



in which the bridges are, firstly, the direct union of the two tertiary carbon atoms (0), secondly, the bridge containing the CH_2 group (1), and thirdly, the bridge, $\cdot CH_2 \cdot CH_2 \cdot$ (2). This hydrocarbon, which is the only possible form of a bridged pentamethylene ring, would therefore be (0 : 1 : 2)-*dicyclopentane*.

It is not possible in this paper to discuss this scheme in its entirety, but the case of the four *cyclo*heptanes given by von Baeyer (whose interesting paper should be consulted for further details) will illustrate its general applicability.

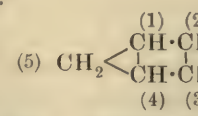
(0 : 1 : 4).

(0 : 2 : 3).

(1 : 2 : 2).

(1 : 1 : 3).

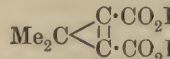
We propose to use this system in naming the derivatives of di*cyclo*pentane which we describe in this paper, and the positions occupied by the various substituting groups will be indicated by numbers according to the scheme.*



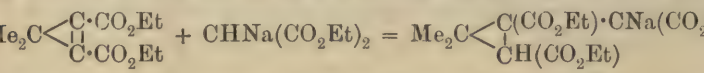
* Starting the numbering at one of the tertiary carbon atoms (compare Baeyer, *loc. cit.*, p. 3774).

But for the sake of brevity in writing names, the numbers will always be omitted where the constitution of the substance referred to is sufficiently clear without numbering, and as there is only one possible di*cyclo*pentane the prefix (0 : 1 : 2) will also be neglected.

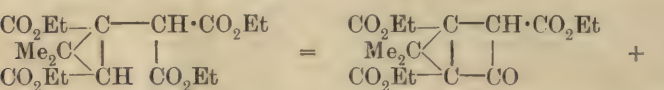
In commencing our experiments on the formation of di*cyclo*pentane derivatives, we endeavoured in the first place to prepare a dimethyltrimethenedicarboxylic ester of the formula



This ester contains a double bond between carbon atoms, both of which are combined with carbethoxy-groups, and might, therefore, be expected to react with the sodium compound of ethyl malonate to form the sodium compound of *ethyl dicarboxydimethyltrimethylenemalonate*,

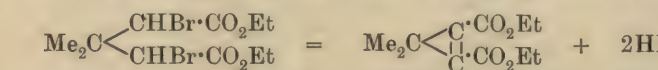


If, then, the ester obtained from this sodium compound by acidifying could be made to undergo condensation with elimination of alcohol, the process might take place thus:

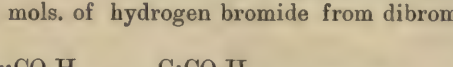


and the condensation product thus formed would be ethyl 5 : 5-dimethyl-3-ketodi*cyclo*pentane-1 : 2 : 4-tricarboxylate.

In order to obtain the dimethyltrimethenedicarboxylic ester necessary for these experiments, we prepared a quantity of *ethyl $a a_1$-dibromo-$\beta\beta$-dimethylglutarate* (p. 754), in the expectation that the elimination of 2 mols. of hydrogen bromide from this would proceed as follows:

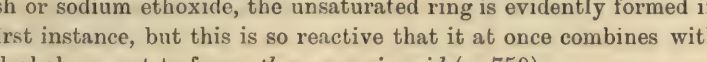


a reaction very similar to the formation of acetylenedicarboxylic acid by the removal of 2 mols. of hydrogen bromide from dibromosuccinic acid.



This reaction seemed the more probable from the consideration of the fact that ethyl monobromodimethylglutarate, under suitable conditions, readily loses hydrogen bromide with formation of ethyl caronate (p. 729). In testing the matter experimentally, we found, however, that even by using the most varied conditions we were unable to isolate a trace of this unsaturated ester or the corresponding acid.

When ethyl dibromodimethylglutarate is digested with alcoholic potash or sodium ethoxide, the unsaturated ring is evidently formed in the first instance, but this is so reactive that it at once combines with the alcohol present to form *ethoxycaronic acid* (p. 759).



In a similar way, if methyl alcoholic potash is employed, the corresponding *methoxycaronic acid* (p. 761) is formed.

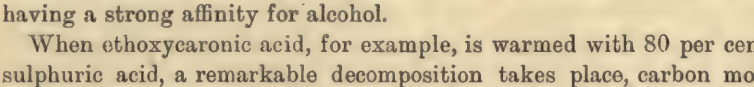
If the dibromo-ester is treated with aqueous potash, part of it is converted into the lactone of dihydroxydimethylglutaric acid (p. 756).

$$CO_2H{\cdot}CH(OH){\cdot}CMe_2{\cdot}CH(OH){\cdot}CO_2H\ ,*$$

and there is also formed some ethoxycaronic acid—an interesting result which shows that the unsaturated ring is so reactive that it even adds on the small quantity of alcohol which is produced by the hydrolysis of the ester, and this in the presence of large quantities of water. Experiments with diethylaniline, silver oxide, and other similar reagents in the place of potash were also made, but in no case could the desired unsaturated substance be isolated.

We were also unsuccessful in our attempts to remove alcohol from ethoxycaronic acid by means of sulphuric acid or other reagents having a strong affinity for alcohol.

When ethoxycaronic acid, for example, is warmed with 80 per cent. sulphuric acid, a remarkable decomposition takes place, carbon monoxide is evolved, and the solution, after adding water, is found to contain *aa*-dimethylsuccinic acid (p. 762). This process, which seems to proceed quantitatively, is probably represented thus:

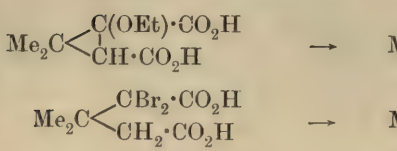


Still more interesting is the behaviour of ethoxycaronic acid on treatment with hydrobromic acid, when it is converted, with disruption of the trimethylene ring, into a bromo-acid, which is evidently *aa-dibromodimethylglutaric acid*, since on boiling with water it is converted into *aa-dihydroxydimethylglutaric acid*. This process may be formulated thus:

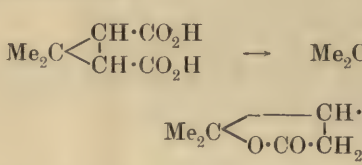
* A very small quantity of *aa*-dihydroxydimethylglutaric acid,

$$CO_2H{\cdot}C(OH)_2{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2H,$$

was also produced in this experiment, which proves that the bromo-ester must have contained traces of ethyl *aa*-dibromodimethylglutarate (see p. 757).



This change is very similar to the conversion of caronic acid into terebic acid by the action of hydrobromic acid (Baeyer and Ipatieff, *Ber.*, 1896, **29**, 2801).

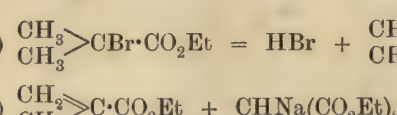


the addition of hydrogen bromide taking place, however, in the two cases in different directions, which is rather curious.

Since we were unable to isolate the unsaturated ester which we required for the synthesis of derivatives of di*cyclo*pentane, we next attempted to use this unsaturated ester in a nascent state, and ultimately we were successful in our endeavours.

In investigations on the behaviour of bromo-esters on treatment with ethyl sodiomalonate and other analogous sodium compounds, it has frequently been noticed that the constitution of the product formed shows that the reaction must have proceeded in two stages. (1) The alkaline sodium compound causes elimination of hydrogen bromide and formation of an unsaturated ester, and (2) the unsaturated ester *at once* combines with a further quantity of the sodium compound present.

Thus, for example, when ethyl *a*-bromo*iso*butyrate is treated with ethyl sodiomalonate, the following reactions occur:



It therefore seemed possible that, under similar circumstances, ethyl dibromodimethylglutarate might first be converted into the unsaturated compound, and that this might then *at once* combine with excess of ethyl sodiomalonate, this addition taking place more rapidly than the addition of alcohol to form ethoxycaronic ester.

The intermediate formation of the unsaturated ester, in this reaction, seemed all the more likely from the fact that when ethyl

dibromodimethylglutarate is treated with sodium ethoxide in alcoholic solution *ethyl ethoxycaronate* is formed.

$$Me_2C\begin{<}CHBr\cdot CO_2Et\\CHBr\cdot CO_2Et\end{>} \rightarrow Me_2C\begin{<}C\cdot CO_2Et\\\|\\C\cdot CO_2Et\end{>} \rightarrow Me_2C\begin{<}C(OEt)\cdot CO_2Et\\|\\CH\cdot CO_2Et\end{>},$$

and not ethyl diethoxydimethylglutarate.

$$CO_2Et\cdot CH(OEt)\cdot CMe_2\cdot CH(OEt)\cdot CO_2Et.$$

On testing this hypothesis experimentally, it was found that a yield of 50—60 per cent. of an ester, which boiled at 234° under 20 mm. pressure, was obtained in this way, and analysis showed that this ester had the composition of the condensation product,

$$Me_2C\begin{<}C(CO_2Et)\cdot CH(CO_2Et)_2\\|\\CH\cdot CO_2Et\end{>} \quad \text{I.}$$

which we were endeavouring to prepare (p. 762).

Before using this ester for synthetical work, however, it was most necessary to carefully prove its constitution, since the reaction between the ethyl sodiomalonate and the dibromo-ester might take place in a different way with formation of a derivative of tetramethylene, exactly as is the case when trimethylene bromide reacts with ethyl sodiomalonate.

$$CH_2\begin{<}CH_2Br\\CH_2Br\end{>} + Na_2C(CO_2Et)_2 = CH_2\begin{<}CH_2\\CH_2\end{>}C(CO_2Et)_2 + 2NaBr$$

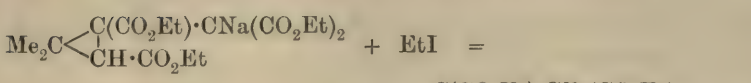
$$Me_2C\begin{<}CHBr\cdot CO_2Et\\CHBr\cdot CO_2Et\end{>} + Na_2C(CO_2Et)_2 =$$

$$Me_2C\begin{<}CH\cdot CO_2Et\\\quad\ >C(CO_2Et)_2\\CH\cdot CO_2Et\end{>} + 2NaBr$$

Ethyl dimethyltetramethylene-tetracarboxylate. II.

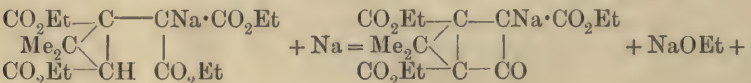
It was not easy to decide between the trimethylene formula, I, and the tetramethylene formula, II, for this ester, but ultimately it was shown in the following way that this substance must be the trimethylene derivative.

If the two possible formulæ are examined, it will be seen that the trimethylene derivative still contains the group $\cdot\overset{*}{C}H(CO_2Et)_2$, and must therefore be capable of forming a sodium compound which should react with alkyl haloids, whereas the tetramethylene derivative contains no such hydrogen atom capable of being replaced by sodium. We therefore treated the ester with sodium ethoxide and ethyl iodide, and obtained at once and in almost quantitative yield the corresponding ethyl derivative.



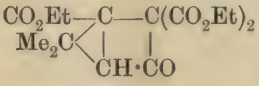
The formation of this ester, a description of the properties of which is given on p. 770, proves conclusively that the product of the action of ethyl dibromodimethylglutarate on the sodium compound of ethyl malonate is *ethyl dicarboxydimethyltrimethylenemalonate* of the constitution represented by formula I.

When this ester, dissolved in boiling xylene, is treated with sodium, or when its alcoholic solution is boiled with sodium ethoxide, a very remarkable reaction takes place, alcohol is eliminated as sodium ethoxide, and a bright yellow, very stable sodium compound is produced. Our experiments seem to us to prove conclusively that the formation of this sodium compound must be expressed in the following way:

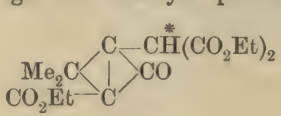


I.

There are two other possible ways in which the ester could undergo internal condensation with elimination of alcohol, that is to say, substances of the following constitutions might conceivably be produced:



II.



III.

The ester (II) contains no hydrogen atom replaceable by sodium and could not therefore yield the yellow sodium compound, which is actually formed in the reaction, and although in formula III the hydrogen atom, H*, would be replaceable by sodium, an extended examination of the substances obtained in various ways from the yellow sodium compound clearly proves that this expression cannot be correct, and that the true constitution of the yellow sodium compound is that represented by formula I and it is therefore the sodium compound of ethyl 5 : 5-dimethyl-3-ketodi*cyclo*pentane-1 : 2 : 4-tricarboxylate.[1]

During the course of this investigation, we discovered that this same yellow sodium compound is directly produced when ethyl dibromodimethylglutarate (1 mol.) is digested in alcoholic solution with 2 mols. of ethyl malonate and 4 mols. of sodium ethoxide (p. 776) and as the yield obtained in this way is 70 per cent. of the theoretical, and the

[1] Dieckmann (*Ber.*, 1900, **33**, 2678) has also expressed the opinion that the formula which we have assigned to this sodium compound is correct.

method is by far the most convenient, it was used in preparing almost the whole of the yellow sodium compound necessary for this research.

In considering the formation of this sodium compound, it should be noted that it is most unusual for alcohol to be eliminated in reactions of this kind in the way represented above, and this is at once evident from a brief consideration of Claisen's work on this subject. In such condensations, as for example, in the formation of ethyl acetoacetate from ethyl acetate, Claisen has shown that the first stage is the addition of sodium ethoxide to the carbethoxy-group of one of the reacting molecules, and that the sodium compound, thus produced, then condenses with the second molecule.

$$(1)\quad CH_3\cdot C\begin{matrix}=O\\ \diagdown OEt\end{matrix} + NaOEt = CH_3\cdot C\begin{matrix}\diagup ONa\\ -Et\\ \diagdown OEt\end{matrix}$$

$$(2)\quad CH_3\cdot C\begin{matrix}\diagup ONa\\ -OEt\\ \diagdown OEt\end{matrix} + CH_3\cdot CO_2Et = CH_3\cdot C(ONa){:}CH\cdot CO_2Et + 2EtOH.$$

Condensations of this nature have, so far, only been known to take place when the conditions necessary for the elimination of 2 molecular proportions of alcohol were present. Thus ethyl acetate condenses with ethyl butyrate, $CH_3\cdot CH_2\cdot \overset{*}{C}H_2\cdot CO_2Et$, but not with ethyl *iso*butyrate, $(CH_3)_2CH\cdot CO_2Et$, because the former does, but the latter does not, contain the two α-hydrogen atoms necessary for the formation of 2 mols. of alcohol according to equation 2.

It is, however, quite conceivable that such condensations may, under favourable circumstances, take place with elimination of only 1 mol. of alcohol according to the scheme,

$$R\cdot C(ONa)(OEt)_2 + R_2CH\cdot CO_2Et - EtOH = R\cdot C(ONa)(OEt)\cdot CR_2\cdot CO_2Et = R\cdot CO\cdot CR_2\cdot CO_2Et + NaOEt,$$

and we believe that the formation of the yellow sodium compound is a case of this kind.

The yellow sodium compound is very sparingly soluble in water, and is only very slowly acted on even by boiling water ; it crystallises from alcohol in bright, orange-yellow, glistening plates and in appearance and several of its properties closely resembles the orange-yellow, crystalline, sodium compound of ethyl dicarboxyglutaconate,

$$(CO_2Et)_2CNa\cdot CH{:}C(CO_2Et)_2,$$

which Conrad and Guthzeit (*Annalen*, 1883, **222**, 250) first prepared by the action of chloroform on ethyl sodiomalonate. Like this substance, the solution of the yellow sodium compound in alcohol gives with ferric chloride an intense reddish-violet coloration.

When the yellow sodium compound is decomposed by acids, a colourless oil is obtained which doubtless consists of *ethyl dimethylketodi*cyclo*pentanetricarboxylate* and if this ester or the sodium compound is left in contact with methyl alcoholic potash, a curious decomposition takes place with formation of the *potassium* compound of *potassium diethyl dimethylketodi*cyclo*pentanetricarboxylate*,

$$Me_2C\begin{cases}C(CO_2Et)\cdot CK\cdot CO_2Et\\ C(CO_2K)-CO\end{cases}.$$

This on acidifying gives the free diethyl hydrogen salt which crystallises in colourless needles melting at 75° and on distillation, loses carbon dioxide with formation of *ethyl dimethylketodi*cyclo*pentanedicarboxylate*,

$$Me_2C\begin{cases}C(CO_2Et)\cdot CH\cdot CO_2Et\\ CH\text{———}CO\end{cases},$$

a colourless oil distilling at 201° under 30 mm. pressure and giving in alcoholic solution an intense reddish-purple coloration with ferric chloride.*

The free acid, which is readily obtained from this ester by hydrolysis with alcoholic potash, is readily soluble in water, melts at 180°, and when its aqueous solution is heated at 180° is decomposed with loss of carbon dioxide and formation of *dimethylketodi*cyclo*pentanecarboxylic acid* (m. p. 180°),

$$Me_2C\begin{cases}C(CO_2H)\cdot CH_2\\ CH\text{———}CO\end{cases},$$

* The behaviour of this ester with ferric chloride, taken in connection with the constitution of the yellow sodium compound, clearly indicates the course of the reaction which takes place in the formation of the dipotassium diethyl salt, and seems to us to prove that the diethyl hydrogen salt (m. p. 75°) obtained by acidifying the dipotassium salt must have the constitution

$$Me_2C\begin{cases}C(CO_2Et)\cdot CH\cdot CO_2Et\\ C(CO_2H)-CO\end{cases}\qquad \text{I.}$$

The other alternative formulæ:

$$Me_2C\begin{cases}C(CO_2H)-CH\cdot CO_2Et\\ C(CO_2Et)\cdot CO\end{cases}\qquad \text{II.}$$

$$Me_2C\begin{cases}C(CO_2Et)\cdot CH\cdot CO_2H\\ C(CO_2Et)\cdot CO\end{cases}\qquad \text{III.}$$

are, in our opinion, not possible, for the following reasons.

In formula II, the carboxyl group is not attached to a carbon atom united to the CO group, and therefore it is unlikely that it would be so readily eliminated as is actually the case; a compound having formula III would, on distillation, yield a diethyl ester which would not be capable of giving a coloration with ferric chloride. Furthermore, it will be seen from the following pages that formula I explains in a satisfactory manner the formation and properties of the numerous substances we have prepared from the diethyl hydrogen salt.

which is sparingly soluble in water and gives no coloration with ferric chloride.

When the yellow sodium compound, instead of being left in contact with methyl alcoholic potash, is boiled with alcoholic potash, it is converted into a mixture of two isomeric dibasic acids, $C_9H_{10}O_5$, melting at 155° and 180°, and called respectively A and B, the latter being identical with the acid of the same melting point mentioned above. Obviously during the hydrolysis the sodium compound is first converted into *dimethylketodi*cyclo*pentanetricarboxylic acid*,

$$Me_2C\begin{cases}C(CO_2H)\cdot CH\cdot CO_2H\ (1),\\ C(CO_2H)\cdot CO\\ \qquad (2)\end{cases}$$

which then loses carbon dioxide with formation of the two isomeric dibasic acids.

If the formula of the tribasic acid is examined, it will be seen that two of the carbon atoms, marked (1) and (2), should be readily eliminated on hydrolysis with potash, since both are attached to carbon atoms joined to a CO group (as in the case of acetoacetic acid, acetonedicarboxylic acid, &c.). If, then, we suppose that different carboxyl groups have been removed in the formation of the isomeric dibasic acids, these would have the following formulæ:

$$Me_2C\begin{cases}C(CO_2H)\cdot CH\cdot CO_2H\\ CH\text{———}CO\end{cases}\qquad \text{I.}$$

$$Me_2C\begin{cases}C(CO_2H)\cdot CH_2\\ C(CO_2H)\cdot CO\end{cases}\qquad \text{II.}$$

and the one having the constitution represented by the first formula would give a coloration with ferric chloride, whereas the other would not. Experiment, however, shows that both the acids give colorations with ferric chloride, that produced in the case of the acid melting at 155° being an intense bluish-violet, whereas the aqueous solution of the acid melting at 180° gives a reddish-violet. Both these acids, when heated, lose 1 mol. of carbon dioxide, and are converted into *dimethylketodi*cyclo*pentanecarboxylic acid*,

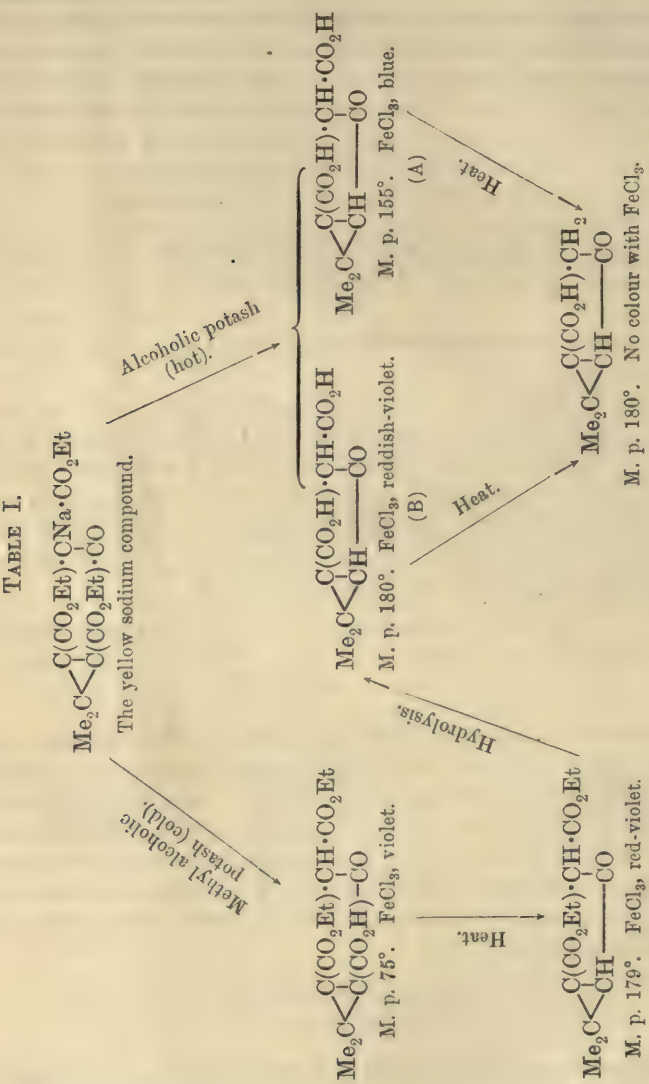
$$Me_2C\begin{cases}C(CO_2H)\cdot CH_2\\ CH\text{———}CO\end{cases},$$

the change taking place in the case of the acid melting at 155° on simply boiling with dilute sulphuric acid, whereas, in the case of the acid melting at 180°, it is necessary to heat with water at 180°. The general behaviour of the two dibasic acids leads us to believe that they are not structurally different, but simply stereoisomeric modifications of the formula I given above.

In order that the relationships between these various substances

may be clearly seen at a glance, we give the following table, showing their methods of formation:

TABLE I.



Oxidation of Dimethylketodicyclopentanecarboxylic Acid,

$$Me_2C\begin{cases}C(CO_2H)\cdot CH_2\\ CH\text{——}CO\end{cases}.$$

In order to obtain as much evidence as possible in favour of the constitution we have assigned to this acid, we next studied its behaviour

on oxidation with nitric acid under various conditions, when it was found to yield, besides *aa-dimethylsuccinic acid*, $CO_2H{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2H$, a new dibasic acid of the formula $C_7H_{10}O_5$ and melting at 84°. For a considerable time, we were unable to discover the nature of this acid, which is the principal product of the oxidation; but ultimately we succeeded in proving conclusively that it has the constitution

$$CO_2H{\cdot}C(OH)_2{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2H,$$

and is therefore *aa-dihydroxy-ββ-dimethylglutaric acid.*

In the first place, we showed that the new acid was not the *aa*$_1$-*dihydroxydimethylglutaric acid*, $CO_2H{\cdot}CH(OH){\cdot}CMe_2{\cdot}CH(OH){\cdot}CO_2H$, by preparing this acid, or rather its lactone,

$$Me_2C\begin{<}\begin{matrix}CH(OH)\text{—}CO\\ CH(CO_2H){\cdot}O\end{matrix},$$

from *aa*$_1$-dibromodimethylglutaric acid by a series of reactions described later (pp. 755, 756).

This lactone melts at 142°, and is quite different in its other properties from the acid melting at 84°. We next found that the new acid of melting point 84°, although it has the formula $C_5H_{10}O_2(CO_2H)_2$, and forms a *calcium* salt, $C_5H_{10}O_2(CO_2)_2Ca$, behaves in many of its reactions as a ketonic acid, $C_4H_8{\cdot}CO(CO_2H)_2$, containing 1 mol. of water less; thus it combines with phenylhydrazine and gives, with *o*-tolylenediamine, a well characterised condensation product derived from an acid of the latter formula.

In its properties, this acid shows considerable similarity to glyoxylic acid which crystallises in prisms having the formula $CH(OH)_2{\cdot}CO_2H$, and forms salts of the general formula $CH(OH)_2{\cdot}CO_2M$. On the other hand, glyoxylic acid shows the properties of the aldehydo-acid, $CHO{\cdot}CO_2H$, containing 1 mol. of water less, since it combines with hydroxylamine to form oximidoacetic acid, $OH{\cdot}N{:}CH{\cdot}CO_2H$, and on treatment with phenylhydrazine is converted into phenylhydrazineglyoxylic acid, $C_6H_5{\cdot}N_2H{:}CH{\cdot}CO_2H$. This striking similarity in properties leads us to the conclusion that in the crystalline state and in its salts this new acid (m. p. 84°) is *aa-dihydroxydimethylglutaric acid*, of the formula

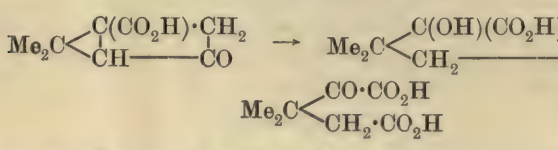
$$CO_2H{\cdot}C(OH)_2{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2H,$$

but that, under suitable conditions, it can react as the corresponding ketonic acid, $CO_2H{\cdot}CO{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2H$. Since glyoxylic acid, on reduction, yields glycollic acid, we investigated the action of reducing agents on our new acid, and found that this behaved in an exactly analogous manner, yielding the *lactone* of *a-hydroxydimethylglutaric acid* (m. p. 112°, p. 758).

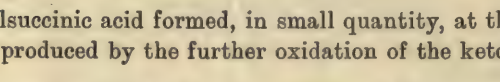
$$\begin{matrix}CH(CO_2H){\cdot}CMe_2{\cdot}CH_2\\ O\text{——————}CO\end{matrix},$$

a substance which we had previously obtained (Trans., 1899, **75**, 56) by the action of sodium carbonate on ethyl hydrogen α-bromodimethylglutarate.

In order to explain the formation of αα-dihydroxydimethylglutaric acid from dimethylketodi*cyclo*pentanecarboxylic acid, it may be assumed that, at one stage of the oxidation, the trimethylene ring is split by the addition of water, and that the hydroxy-derivative formed is further oxidised to the ketonic acid, thus:



The dimethylsuccinic acid formed, in small quantity, at the same time is evidently produced by the further oxidation of the ketonic acid,

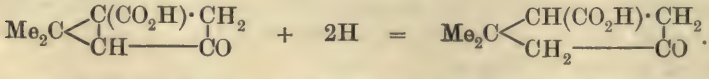


The formation of αα-dihydroxydimethylglutaric acid from ethoxycaronic acid by the action of hydrobromic acid (p. 762) and from αα-dibromodimethylglutaric acid by means of sodium carbonate subsequently placed the constitution of this acid beyond question.

*Reduction of Dimethylketodi*cyclo*pentanecarboxylic Acid.*

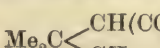
When this acid is treated with sodium amalgam (p. 782), it readily takes up two hydrogen atoms, with formation of an acid of the formula $C_8H_{12}O_3$ (m. p. 103°), which at first was thought to be the corresponding hydroxy-acid.

Since, however, the reduced acid yields a well characterised *semicarbazone*, it obviously still contains a ketonic group, and this fact, taken in connection with the other properties of the acid, shows that the two atoms of hydrogen which have been taken up have severed the trimethylene ring, this curious change occurring before the reduction of the ketonic group.

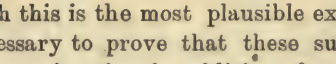


The acid $C_8H_{12}O_3$, which is therefore *dimethylketopentamethylenecarboxylic acid*, is not easily acted on by sodium amalgam, but if a

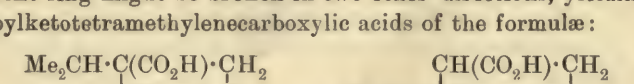
large excess is employed, it is ultimately reduced to the corresponding *hydroxydimethylpentamethylenecarboxylic acid* (m. p. 115°).



Although this is the most plausible expanation of these facts, it was still necessary to prove that these substances were pentamethylene derivatives, since by the addition of two atoms of hydrogen the trimethylene ring might be broken in two other directions, yielding two *iso*propylketotetramethylenecarboxylic acids of the formulæ:



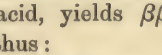
It was fortunately found to be a comparatively easy matter to prove that the constitution assigned to dimethylketodi*cyclo*pentanecarboxylic acid is correct, since experiment showed that this acid, on oxidation with nitric acid, yields *ββ*-dimethylglutaric acid and *αα*-dimethylsuccinic acid thus:



This process is exactly similar to that which has repeatedly been observed in the case of the oxidation of *cyclo*ketonic compounds; thus nitric acid oxidises ketopentamethylene to glutaric acid (Wislicenus and Hentzschel, *Annalen*, 1893, **275**, 321), and ketohexamethylene to adipic acid (Wislicenus and Mager, *ibid.*, 363), and the formation of dimethylglutaric acid in the above oxidation clearly shows that dimethylketodi*cyclo*pentanecarboxylic acid cannot be a derivative of *iso*propylketotetramethylene.

Action of Methyl Iodide on the Yellow Sodium Compound.

When the yellow sodium compound, suspended in methyl alcohol, is boiled with methyl iodide, decomposition readily takes place with elimination of sodium iodide and formation of *ethyl* 5 : 5 : 2-*trimethylketodi*cyclo*pentanetricarboxylate* (p. 786).

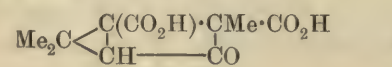


a colourless oil which distils constantly at 219° under 20 mm. pressure.

This ester on hydrolysis with methyl alcoholic potash in the cold is converted into the corresponding colourless, crystalline potassium salt

of the formula $C_8H_9O(CO_2K)_3$, and this when acidified is decomposed with elimination of carbon dioxide and formation of a crystalline acid melting at 146°.

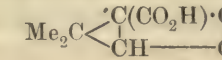
Since this acid is dibasic, its constitution may be represented by either of the formulæ



I. II.

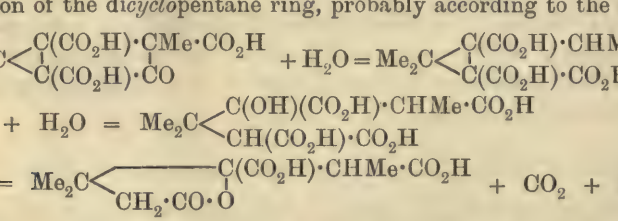
and although we consider I the more probable, the evidence at our disposal is not sufficient to enable us to definitely decide between the two possibilities.

When the solution of the dibasic acid in water is heated at 180°, it is decomposed into carbon dioxide and *trimethylketodi*cyclo*pentanecarboxylic acid*,



a crystalline acid which melts at 134°, is sparingly soluble in water and, as a ketonic acid, readily yields a semicarbazone.

Quite unexpected and very interesting results were obtained in investigating the action of boiling ethyl alcoholic potash on ethyl trimethylketodi*cyclo*pentanetricarboxylate. The product of this reaction, which is a substance sparingly soluble in water and melting at 237°, has been clearly proved to be the *lactone* of *hydroxytrimethylbutanetricarboxylic acid* (p. 788), and it must be assumed that in its formation 2 mols. of water have been taken up with consequent complete disruption of the di*cyclo*pentane ring, probably according to the scheme:



In formulating the process in this way, we have been guided by the following properties of the acid:

(1) It is a dibasic lactonic acid which yields a *silver* salt, $C_{10}H_{12}O_6Ag_2$, and when boiled with baryta it is hydrolysed with formation of the tribasic *barium* salt, $C_{20}H_{26}O_{14}Ba_3$.

(2) The difficulty with which it is hydrolysed on boiling with water indicates that it is most probably a γ-lactone.

(3) When treated with acetyl chloride, it is converted into an anhydride melting at 94—96°, and this on treatment with alkalis yields again the same acid melting at 237°. The ease with which this an-

hydride is formed points to the probability of the two carbon atoms being attached to neighbouring carbon atoms, as in succinic acid.

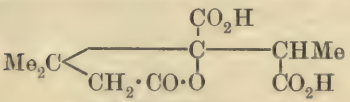
All these points are brought out in the formula represented above.

It is, however, obvious that disruption of the trimethylene ring may take place in other ways with formation, for example, of a substance of the formula

$$\begin{matrix} Me_2CH\cdot C(CO_2H)\cdot CHMe \\ CO_2H\cdot CH\text{—}O\text{—}CO \end{matrix}$$

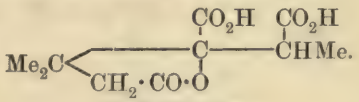
We hope to be able, at a later stage, to investigate the decomposition of this and other similar lactones described in this paper by fusion with potash (Baeyer, *Ber.*, 1896, **29**, 2795), in order to definitely prove their constitution.

When the lactonic acid melting at 237° is distilled under diminished pressure and the distillate boiled with water, an isomeric acid melting at 181° is obtained, which on treatment with acetyl chloride yields an anhydride melting at 131°. This anhydride on boiling with water is again converted into the acid melting at 181°. From this behaviour, it is obvious that this lactone of hydroxytrimethylbutanetricarboxylic acid exists in two isomeric forms, which may be represented thus:



trans-Modification.

Acid melts at 237°.
Anhydride melts at 96°.



cis-Modification.

Acid melts at 181°.
Anhydride melts at 131°.

These lactonic acids are very similar in constitution to the lactones of cis- and trans-*hydroxycamphoronic acid*, $\begin{matrix} Me_2C\text{—}CO\text{—}O \\ MeC(CO_2H)\cdot CH\cdot CO_2H \end{matrix}$ (Bredt, *Annalen*, 1898, **299**, 136), which also yield anhydrides. They have also many points in common with the lactone of *a-hydroxydimethyltricarballylic acid*, $\begin{matrix} Me_2C\cdot CH(CO_2H)\cdot CH\cdot CO_2H \\ CO\text{————}O \end{matrix}$ (Baeyer, *Ber.*, 1896, **29**, 2794).

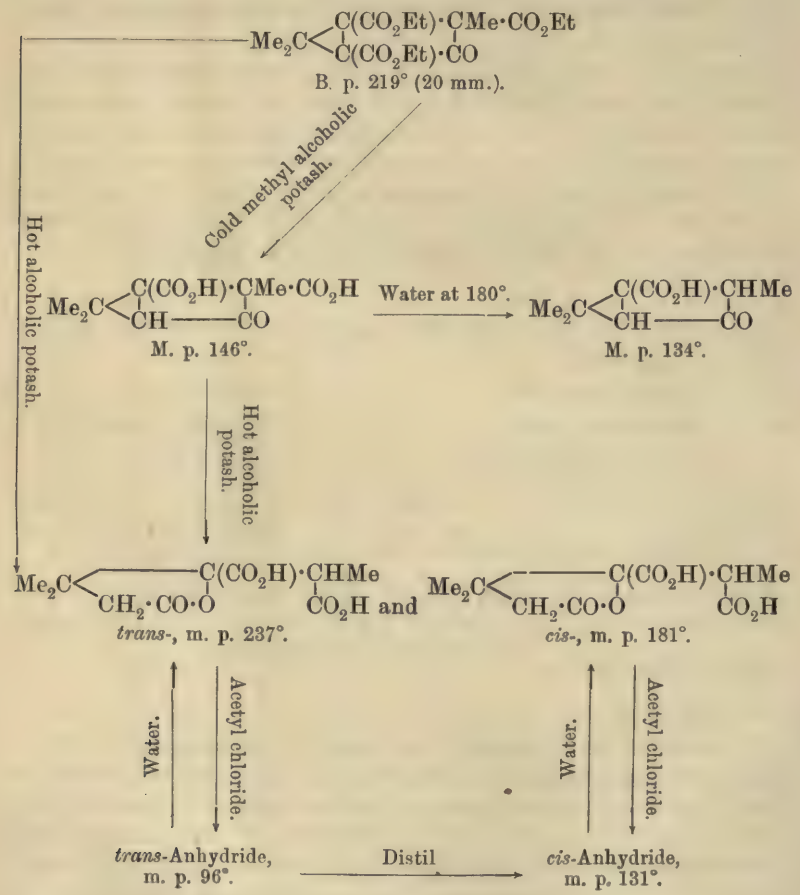
In searching the literature for examples of the disruption of the trimethylene ring by means of alkali, we have been able to find only one case, which, however, is of an almost identical nature with that described above. Buchner and Witter (*Ber.*, 1894, **27**, 871) found that methyl dicarboxytrimethyleneacetate, when hydrolysed with caustic soda, did not yield the corresponding acid, but was converted, with disruption of the trimethylene ring and loss of carbon dioxide, into a dibasic lactonic acid (Paraconcarbonessigsäure).

$CO_2Me\cdot CH_2\cdot C(CO_2H)<^{CH\cdot CO_2Me}_{CH\cdot CO_2Me}$ gives

$CO_2H\cdot CH_2\cdot CH<^{\text{———}CH\cdot CO_2H}_{CH_2\cdot CO\cdot O}$.

In order that our interpretation of the somewhat complicated decompositions, which are described above, may be clearly understood, we append a table of the various substances which have been obtained from the product of the action of methyl iodide on the yellow sodium compound:

TABLE II.



Examination of the Behaviour of Ethyl Dicarboxydimethyltrimethylene-malonate, $Me_2C<^{C(CO_2Et)\cdot CH(CO_2Et)_2}_{CH\cdot CO_2Et}$.

When this ester is digested with alcoholic potash, it yields two isomeric substances, $C_9H_{12}O_6$, which melt, or rather decompose, at 158° and 188° respectively, and both of which are *dibasic lactonic acids.* The behaviour of this ester with alcoholic potash is thus very similar to that just described in the case of ethyl trimethylketodi*cyclo*pentanetricarboxylate, the trimethylene ring suffering disruption under the influence of the alkali. The constitution of these two lactonic acids may very probably be expressed by the formulæ

$$Me_2C<^{C(CO_2H)\cdot CH_2\cdot CO_2H}_{CH_2\cdot CO\cdot O}$$ I.

$$Me_2C<^{CH(CH_2\cdot CO_2H)}_{CH(CO_2H)-O}>CO,$$ II.

which represent them as structurally isomeric *lactones* of two *hydroxydimethylbutanetricarboxylic acids.* When these acids are heated, they decompose readily with evolution of carbon dioxide and formation of two different monobasic lactonic acids, $C_8H_{12}O_4$, which melt at 154° and 108° respectively.*

Arguing by analogy, it is most probable that the carboxyl group, which is eliminated from I in this process, is that which is attached to the tertiary carbon atom, especially as that atom is also united to the oxygen atom of the lactone ring. The *lactone* of *hydroxydimethylbutanedicarboxylic acid* obtained from I will then be

$$Me_2C<^{CH\cdot CH_2\cdot CO_2H}_{CH_2\cdot CO\cdot O}$$ III.

With regard to formula II, there are two possible monobasic lactonic acids which may result from the elimination of carbon dioxide, namely,

$$Me_2C<^{CH(CH_2\cdot CO_2H)}_{CH_2-O}>CO$$ IV.

$$Me_2C<^{CH(CH_3)}_{CH(CO_2H)\cdot O}>CO,$$ V.

but of these two possibilities, the lactonic acid represented by V has already been prepared by Balbiano (*Ber.*, 1894, **27**, 2136; 1895, **28**, 1508; compare Mahla and Tiemann, *Ber.*, 1895, **28**, 2161), it melts at 164°, and is, apparently, different from the acid obtained by us. We are, therefore, of opinion that the constitutions of the *lactones* of the two *hydroxybutanecarboxylic acids* melting at 158° and 188° are re-

* If the acid melting at 158° and 188° had been stereoisomeric as in the case of their methyl derivatives (p. 745), they would doubtless have been converted into the same acid by the action of heat and elimination of carbon dioxide.

presented by I and II, but we have not, as yet, sufficient evidence to enable us to decide which of these belongs to the substance of melting point 158° and which to that of melting point 188°; we propose, in the meantime, to name the first of these *A* and the second *B*. Similarly, we propose to name the monobasic lactonic acids melting at 154° and 108°, which are probably represented by III and IV, the lactones of *A*- and *B-hydroxydimethylbutanedicarboxylic acid.*

When ethyl dicarboxydimethyltrimethylenemalonate is treated with bromine, it is readily attacked with evolution of hydrogen bromide and formation of *ethyl dicarboxydimethyltrimethylenebromomalonate* (p. 769),

$$Me_2C<\begin{matrix}C(CO_2Et)\cdot CBr(CO_2Et)_2\\ CH\cdot CO_2Et\end{matrix},$$

and we have carefully studied the action of alcoholic potash on this compound, in the hope that hydrogen bromide might be eliminated in the apparently only possible direction, with formation of the acid,

$$Me_2C<\begin{matrix}C-CO_2H\\ \|\quad C(CO_2H)_2,\\ C-CO_2H\end{matrix}$$

which is a derivative of *dicyclotetrane.*

We obtained in this way a monobasic anhydro-acid melting at 207°, which, on treatment with alkalis, is converted into a tribasic acid. Since this substance has the formula $C_9H_{10}O_5$, it is probably *anhydrodimethyltetramethylenetricarboxylic acid,*

$$Me_2C<\begin{matrix}CH(CO_2H)\cdot CH\cdot CO\\ \qquad\qquad\quad CH\cdot CO\end{matrix}>O,$$

reduction of the di*cyclo*tetrane ring having taken place during hydrolysis. This reaction is being further investigated.

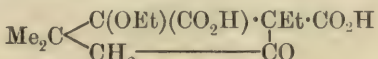
Investigation of Ethyl Dicarboxydimethyltrimethylene-ethylmalonate,

$$Me_2C<\begin{matrix}C(CO_2Et)\cdot CEt(CO_2Et)_2\\ CH\cdot CO_2Et\end{matrix}$$

The principal product of the action of alcoholic potash on this ester is a crystalline substance, $C_{13}H_{20}O_6$, which melts at 175°, and the silver salt of which has the formula $C_{13}H_{18}O_6Ag_2$; we were thus, in the first instance, led to suppose that hydrolysis had not been complete, and that this substance was the ethyl dihydrogen salt of the acid,

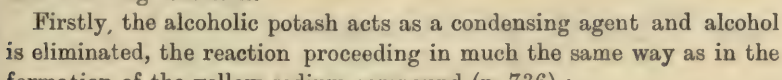
$$Me_2C<\begin{matrix}C(CO_2H)\cdot CHEt\cdot CO_2H\\ CH\cdot CO_2H\end{matrix}.$$

Since, however, prolonged boiling with caustic alkalis did not further hydrolyse the substance, we were obliged to abandon this view, and further investigation has led us to the conclusion that this remarkable compound is *ethoxydimethylethylketopentamethylenedicarboxylic acid*,

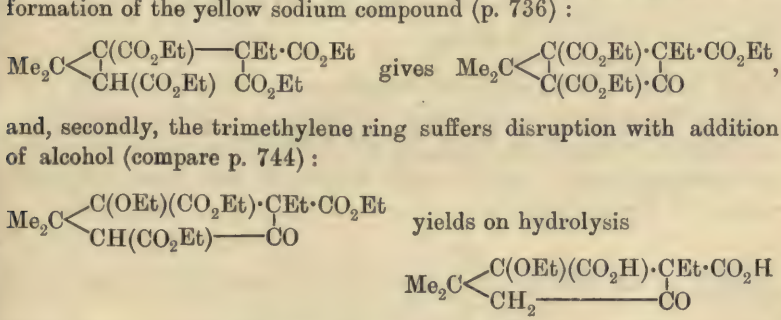


The formation of such a substance may be assumed to be the result of the following reactions.

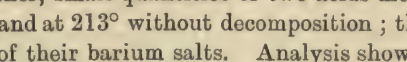
Firstly, the alcoholic potash acts as a condensing agent and alcohol is eliminated, the reaction proceeding in much the same way as in the formation of the yellow sodium compound (p. 736) :



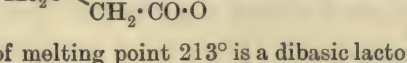
and, secondly, the trimethylene ring suffers disruption with addition of alcohol (compare p. 744) :



Remarkable as this reaction undoubtedly is, we do not see any other way of explaining the composition and properties of the substance melting at 175°. The mother liquors of this substance yield, on extraction with ether, small quantities of two acids melting at 193° with decomposition, and at 213° without decomposition ; these can be separated by means of their barium salts. Analysis shows that the former has the formula $C_{12}H_{26}O_8$, and the results of titration prove conclusively that it is a tribasic lactonic acid ; there can thus be little doubt that it is the *lactone* of *hydroxydimethylethylbutanetetracarboxylic acid*,



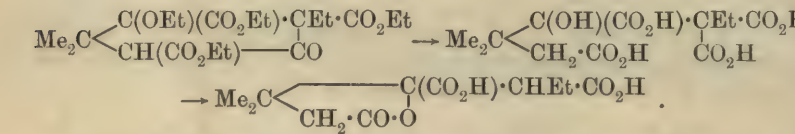
The substance of melting point 213° is a dibasic lactonic acid, $C_{11}H_{16}O_6$, and therefore very probably one of the stereoisomeric modifications of the *lactone* of *hydroxydimethylethylbutanetricarboxylic acid*,



and as it shows little tendency to form an anhydride, and melts higher than the isomeride to be mentioned immediately, we have provisionally named it *trans-*.

Although the ethoxypentamethylene derivative of melting point

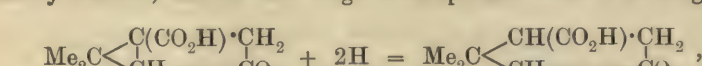
175° is so stable towards alkalis, it is readily attacked by boiling concentrated hydrochloric acid, with formation of a beautifully crystalline lactone dibasic acid, $C_{11}H_{16}O_6$, which melts at 153°, and is evidently the *cis*-modification of the *lactone* of *hydroxydimethylethylbutanetricarboxylic acid*. The formation of this dibasic lactonic acid is readily understood, if the constitution of the substance melting at 175°, which is given above, is accepted, and indeed this decomposition was one of the strong reasons which induced us to adopt this constitution.



When heated a little above its melting point, or when treated with acetyl chloride, the dibasic lactonic acid melting at 153° is readily converted into its anhydride, $C_{11}H_{14}O_5$, which on boiling with water again regenerates the same acid; for this reason, we have named this substance the *cis*-modification.

*Stability of the Ketodi*cyclo*pentane Ring, especially as compared with that of the Trimethylene Ring.*

The study of the action of reagents on the carboxylic acids of dimethylketodi*cyclo*pentane has brought to light some remarkable changes which show the instability of a bridged ring of this nature under conditions which do not usually lead to the disruption of a saturated ring. In this connection, two reactions only need be mentioned, namely, the behaviour of *dimethylketodi*cyclo*pentanecarboxylic acid* (p. 742) 1, on reduction, and 2, on oxidation (p. 740); other decompositions bearing on this interesting point will be readily noticed, especially in reading the experimental part of this paper. It has already been mentioned that dimethylketodi*cyclo*pentanecarboxylic acid is very readily reduced, and the first stage of the process is the following:



that is to say, disruption of the trimethylene ring actually takes place before the reduction of the ketonic group, and this seems to us to show that in forming a bridge in the *cyclo*pentane (pentamethylene) ring, the strain produced is so great that nascent hydrogen at the ordinary temperature is able to bring about its dissolution. The unstable nature of the bridge is further emphasised by the study of the behaviour of dimethylketodi*cyclo*pentanecarboxylic acid on oxidation,

when, instead of yielding, as we expected, a trimethylene derivative, thus :

$$Me_2C<\begin{matrix}C(CO_2H)\cdot CH_2\\ |\quad\quad |\\ CH\text{——}CO\end{matrix} \quad \text{gives} \quad Me_2C<\begin{matrix}C(CO_2H)\cdot CO_2H\\ |\\ CH\cdot CO_2H\end{matrix},$$

a reaction which would be exactly analogous to the formation of glutaric acid by the oxidation of ketopentamethylene,

$$CH_2<\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CO\end{matrix} \quad \text{gives} \quad CH_2<\begin{matrix}CH_2\cdot CO_2H\\ |\\ CH_2\cdot CO_2H'\end{matrix}$$

the reaction proceeds with disruption of the trimethylene ring and formation of *aa*-dihydroxydimethylglutaric acid,

$$Me_2C<\begin{matrix}C(CO_2H)\cdot CH_2\\ |\quad\quad |\\ CH\text{——}CO\end{matrix} \quad \text{gives} \quad Me_2C<\begin{matrix}CH_2\cdot CO_2H\\ |\\ C(OH)_2\cdot CO_2H\end{matrix}.$$

The stability of the trimethylene ring has been made the subject of much investigation, and it is interesting to contrast the stability of the simple ring with that of the same ring in combination with a tetramethylene ring, as is the case in the di*cyclo*pentane derivatives described in this paper.

The most striking difference which is at once apparent is the fact that the trimethylene ring exhibits an unusual degree of stability towards reducing and oxidising agents. Thus, the trimethylenedicarboxylic acids,

$$\begin{matrix}CH_2\\ |\\ CH_2\end{matrix}>C(CO_2H)_2 \quad \text{and} \quad CH_2<\begin{matrix}CH\cdot CO_2H\\ |\\ CH\cdot CO_2H'\end{matrix}$$

are neither oxidised by permanganate nor reduced when treated with sodium amalgam, and in describing the caronic acids,

$$Me_2C<\begin{matrix}CH\cdot CO_2H\\ |\\ CH\cdot CO_2H\end{matrix}$$

(which are more closely allied to the substances described in this paper), Baeyer and Ipatieff (*Ber.*, 1896, **29**, 2798—2800) particularly emphasise their great stability towards oxidising and reducing agents. It is obvious, then, that the simple trimethylene ring is much more stable than the three-carbon ring in di*cyclo*pentane, and this we consider may be well explained by the assumption that in the latter hydrocarbon the bridge is produced under great strain, and therefore easily suffers disruption when treated with suitable reagents.

From this it follows that, in many cases, it will not be possible to predict, with any degree of certainty, the properties of a polycyclic compound from the consideration of the stability of the rings of which it is composed. Indeed, this is already apparent from the study of

many of the reactions of those members of the terpene series which are supposed to contain dicyclic rings.

During the course of our investigation of the derivatives of di*cyclo*pentane, we have had occasion to prepare and examine some interesting derivatives of $\beta\beta$-dimethylglutaric acid, $CO_2H\cdot CH_2\cdot CMe_2\cdot CH_2\cdot CO_2H$, and the results of these experiments may conveniently be briefly summarised as follows:

$\alpha\alpha_1$-Dibromodimethylglutaric acid, $CO_2H\cdot CHBr\cdot CMe_2\cdot CHBr\cdot CO_2H$, is obtained by treating dimethylglutaric acid with phosphorus pentachloride and bromine and digesting the product with anhydrous formic acid. It melts at 187—189°, and when treated with pyridine or boiled with water it yields the *lactone* of *α-bromo-α_1-hydroxy-$\beta\beta$-dimethylglutaric acid*.

$$Me_2C\begin{cases}CHBr\text{———}CO\\ CH(CO_2H)\cdot O\end{cases}.$$

This melts at 169—170°, gives an ethyl ester boiling at 201° under 45 mm. pressure, and is characterised by the great stability of its bromine atom, which is not removed by boiling with silver nitrate and nitric acid. When, however, the bromolactone is boiled with strong potash, it yields the corresponding *lactone* of *$\alpha\alpha_1$-dihydroxy-$\beta\beta$-dimethylglutaric acid*,

$$Me_2C\begin{cases}CH(OH)\text{—}CO\\ CO(CO_2H)\cdot O\end{cases},$$

which melts at 142°, and seems to have little tendency to form a double lactone.

When *$\beta\beta$-dimethylglutaric acid* is brominated, the principal product is the $\alpha\alpha_1$-dibromo-acid mentioned above, but, at the same time, a small quantity of the $\alpha\alpha$-dibromo-acid, $CO_2H\cdot CBr_2\cdot CMe_2\cdot CH_2\cdot CO_2H$, is always formed, and on pouring the product of bromination into alcohol, the former is completely converted into the diethyl ester, whereas the latter yields, curiously enough, only the ethyl hydrogen salt which probably has the composition $CO_2H\cdot CBr_2\cdot CMe_2\cdot CH_2\cdot CO_2Et$.

This, when boiled with sodium carbonate, yields *$\alpha\alpha$-dihydroxydimethylglutaric acid*, an acid which, as has already been mentioned (p. 757), had been obtained in quite a different way, namely, by the oxidation of dimethylketodi*cyclo*pentanecarboxylic acid; the formation of the $\alpha\alpha$-dibromo-acid in the above example leads us to expect that when other dibasic acids containing two CH_2 groups (or a CH_2 and a CH group) next the carboxyl groups are brominated, besides the $\alpha\alpha_1$-dibromo-acid, which is probably in all cases the principal product of the reaction, a certain quantity of the $\alpha\alpha$-dibromo-acid will also be found to be produced.

Thus, in the case of the bromination of succinic acid, for

example, the product may very probably consist of the two acids $CO_2H{\cdot}CHBr{\cdot}CHBr{\cdot}CO_2H$ and $CO_2H{\cdot}CBr_2{\cdot}CH_2{\cdot}CO_2H$, the latter being present in such small quantity that it has so far been overlooked.

In publishing this paper, we do so in order to place on record the mass of facts which has gradually accumulated, but we are, nevertheless, well aware that there is still much that is doubtful, particularly in regard to the constitutions of the various lactones described. We hope at a later date, as the result of further experimental investigation, to be able to clear up these difficulties.

During the four years which were required for carrying out this investigation, we have received most valuable help from Messrs. F. H. Lees and J. Yates, to the latter of whom, especially, most of the analyses given in this paper are due. Our thanks are also due to Mr. C. Walker for his assistance in the preparation of a considerable quantity of the necessary material.

We wish also to state that much of the heavy expense, which is unavoidable in an investigation of this kind, has been met by repeated grants from the Government Grant Fund of the Royal Society.

Experimental.

Part I. Derivatives of ββ-Dimethylglutaric Acid: Formation of Ethyl Dimethyltrimethylenemalonate and its Derivatives.

By W. H. Perkin, jun., and J. F. Thorpe.

Preparation of ββ-Dimethylglutaric Anhydride, $Me_2C\langle\begin{matrix}CH_2{\cdot}CO\\CH_2{\cdot}CO\end{matrix}\rangle O$. —When ethyl sodiocyanoacetate is condensed in alcoholic solution, with ethyl dimethylacrylate, the product consists for the most part of ethyl hydrogen α-cyano-ββ-dimethylglutarate,

$$CO_2H{\cdot}CH(CN){\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2Et,$$

which is converted by hydrolysis with sulphuric acid into ββ-dimethylglutaric acid (Trans., 1899, **75**, 52, 54).

In preparing, from the ethyl hydrogen cyano-ester, the large quantities of dimethylglutaric anhydride which were necessary for this research, we found the following process to give the best results.

The crude cyano-ester is heated with twice its volume of 50 per cent. sulphuric acid until all oil has passed into solution, the operation being conducted in a flask connected with an air condenser so that the alcohol formed can escape; from time to time, small quantities of

water are added to keep the liquid at its original volume. The product is mixed with a saturated solution of ammonium sulphate, extracted several times with ether, the ethereal solution dried over calcium chloride and evaporated, when a dark brown, crystalline cake of crude dimethylglutaric acid is obtained. This is boiled with an equal volume of acetic anhydride for 2 hours; the acetic acid and the excess of acetic anhydride are then distilled off as far as possible under the ordinary pressure and the residue fractionated under 30 mm. pressure, when almost the whole of the anhydride passes over at 180—190°, and immediately solidifies in the receiver. In order to further purify this, advantage is taken of the fact that the anhydride is sparingly soluble in dry ether, so that, if the crude product is ground up with dry ether, the impurities dissolve, leaving a residue of colourless crystals of the pure anhydride.

The impurities extracted by the ether contain nitrogen, and after distilling off the ether, the residue is again boiled with dilute sulphuric acid and the whole process repeated as given above, when a further considerable quantity of pure anhydride is easily obtained. The properties of this compound have already been given (Trans., 1896, **69**, 1475).

Bromination of ββ-Dimethylglutaric Anhydride. Formation of Ethyl $a a_1$*-Dibromo-ββ-dimethylglutarate,* $CO_2Et{\cdot}CHBr{\cdot}CMe_2{\cdot}CHBr{\cdot}CO_2Et$, *and Ethyl Hydrogen* $a a$*-Dibromo-ββ-dimethylglutarate,* $CO_2H{\cdot}CBr_2{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2Et$ (?).

As mentioned in the introduction, ββ-dimethylglutaric anhydride, when treated with phosphorus and bromine, is both symmetrically and unsymmetrically brominated, the proportions of the former product to the latter being approximately five to one. The conditions under which we always carried out this bromination were as follows.

Pure dimethylglutaric anhydride (100 grams) was mixed with 300 grams of phosphorus pentabromide and the mixture warmed on the water-bath until all had become liquid. Bromine (225 grams) was then gradually added and the whole heated on the water-bath until nearly colourless, a process lasting usually from 5—6 hours. The product, after cooling, was poured into four times its volume of absolute alcohol and the whole allowed to stand for 12 hours. The oil, which separated on adding water, was extracted with ether, washed with water and dilute sodium carbonate, and dried over calcium chloride. The ethereal solution on evaporating yielded 216 grams of *ethyl* $a a_1$*-dibromodimethylglutarate* as a colourless liquid boiling at 194° under 30 mm. pressure.

0·5336 gram gave 0·4213 AgBr. Br = 42·53.

$C_{11}H_{18}O_4Br_2$ requires Br = 42·79 per cent.

The sodium carbonate washings of the ethereal solution (see above) on acidifying gave a thick oil; this was extracted with ether, the ethereal solution washed with water, dried over calcium chloride, and evaporated, when an oil was obtained which, from the results of analysis and its behaviour on boiling with sodium carbonate, is evidently *ethyl hydrogen αα-dibromo-ββ-dimethylglutarate*; it is a thick oil which does not distil without decomposition.

0·1976 gram gave 0·2134 AgBr. Br = 46·5.

$C_9H_{14}O_4Br_2$ requires Br = 46·2 per cent.

The constitution of this substance is proved by its conversion into $\alpha\alpha_1$-dihydroxydimethylglutaric acid, $CO_2H\cdot C(OH)_2\cdot CMe_2\cdot CH_2\cdot CO_2H$, by treatment with sodium carbonate (p. 757).

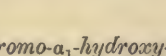
$\alpha\alpha_1$-Dibromo-ββ-dimethylglutaric Acid, $CO_2H\cdot CHBr\cdot CMe_2\cdot CHBr\cdot CO_2H$ is best prepared in the following way. The dibromo-acid bromide, prepared by brominating dimethylglutaric anhydride with the theoretical quantity of bromine and phosphorus pentabromide, as explained above, is poured into an equal volume of glacial formic acid, and the mixture heated on the water-bath until all has dissolved. On cooling, a large quantity of a crystalline solid separates, which can be collected and recrystallised from glacial formic acid, from which it is obtained in the form of large, colourless prisms melting at 187—189° with charring and evolution of gas.

0·1827 gave 0·2129 AgBr. Br = 49·9.

$C_7H_{10}O_4Br_2$ requires Br = 50·2 per cent.

Dibromodimethylglutaric Acid is readily soluble in hot water and separates from the solution unchanged if the operation is rapidly conducted, but since on boiling with water it is gradually decomposed with formation of the lactone of bromohydroxydimethylglutaric acid (see below), it is best to recrystallise it from formic acid.

Lactone of α-Bromo-α_1-hydroxy-ββ-dimethylglutaric Acid,



When dibromodimethylglutaric acid is mixed with excess of pyridine, a considerable development of heat occurs, and if the solution is boiled for two minutes, then cooled, and poured into excess of hydrochloric acid, the above lactone is obtained as a white, crystalline mass on extracting with ether. The same bromolactone is also gradually formed when the dibromo-acid is boiled with water, complete decomposition of the dibromo-acid being brought about after boiling for 12 hours.

Since, however, the bromolactone, during this process, undergoes further change and is partially converted into the hydroxylactone (see below), the pyridine method of preparation is to be preferred. The same bromolactone is also formed when dibromodimethylglutaric acid suspended in water is treated with moist silver oxide.

The *lactone of bromohydroxydimethylglutaric acid* separates from hot water, in which it is readily soluble, in large, transparent prisms and melts at 169—170°. It is a remarkably stable substance which distils unchanged and is unacted on by fuming nitric acid, or by boiling for 12 hours with pyridine.

0·1811 gave 0·2373 CO_2 and 0·0678 H_2O. C = 35·7; H = 4·1.
0·1919 „ 0·2459 CO_2 „ 0·0690 H_2O. C = 35·0; H = 4·0.
$C_7H_9O_4Br$ requires C = 35·4. H = 3·8 per cent.

Since no trace of silver bromide was formed when this bromolactone was boiled with fuming nitric acid and nitrate of silver, the substance was analysed for bromine by fusing it with potassium nitrate and carbonate.

0·2113 gave 0·1659 AgBr. Br = 33·5.
$C_7H_9O_4Br$ requires Br = 33·7 per cent.

The *ethyl* ester, $Me_2C<\begin{matrix}CHBr\text{———}CO\\ CH(CO_2Et)\cdot O\end{matrix}$, is readily obtained by boiling the alcoholic solution of the bromolactone with 10 per cent. of concentrated sulphuric acid on the water-bath for 12 hours. It is a mobile oil which distils without decomposition at 201° under 45 mm. pressure.

0·1778 gave 0·2698 CO_2 and 0·0846 H_2O. C = 41·3; H = 5·2.
0·3421 „ 0·2417 AgBr. Br = 30·1.
$C_9H_{13}O_4Br$ requires C = 40·7; H = 4·9; Br = 30·2 per cent.

Lactone of $\alpha\alpha_1$*-Dihydroxy-*$\beta\beta$*-dimethylglutaric Acid,*

$$Me_2C<\begin{matrix}CH(OH)\text{—}CO\\ CH(CO_2H)\cdot O\end{matrix},$$

Although the bromolactone just described is extremely stable towards acids, it is readily acted on by alkalis, and boiling for 2 hours with a 25 per cent. solution of aqueous potash is sufficient to completely transform it into the above lactone. This compound is very soluble in water; it distils without decomposition, and on warming with concentrated sulphuric acid evolves carbon monoxide. For analysis, the substance was crystallised from dry ether, from which it separates in long needles melting at 140—142°.

0·1682 gave 0·2967 CO_2 and 0·0884 H_2O. C = 48·1 ; H = 5·8.
$C_7H_{10}O_5$ requires C = 48·3 ; H = 5·7 per cent.

The *silver* salt, $C_7H_{10}O_6Ag_2$, of the dihydroxy-acid is obtained when silver nitrate is added to a warm neutral solution of the lactone in ammonia, as a white, crystalline powder moderately soluble in water,

0·3522 gave 0·1866 Ag. Ag = 52·8.
$C_7H_{10}O_6Ag_2$ requires Ag = 53·0 per cent.

When calcium chloride is added to the neutral solution of the ammonium salt, an insoluble calcium salt is thrown down, which may with advantage be used for the isolation of the lactone of the dihydroxy-acid from mixtures with other substances.

αα-Dihydroxy-ββ-dimethylglutaric Acid,
$CO_2H\cdot C(OH)_2\cdot CMe_2\cdot CH_2\cdot CO_2H$.

When ethyl hydrogen αα-dibromodimethylglutarate (p. 755) is dissolved in sodium carbonate solution and boiled, care being taken to keep the solution faintly alkaline throughout the process, it is found that, after 2 hours, no oil is precipitated on acidifying.

If the acidified solution is then saturated with ammonium sulphate and repeatedly extracted with ether, a gummy acid is obtained from the ethereal solution on evaporation which, when dissolved in excess of ammonia and mixed with calcium chloride solution, slowly deposits a large quantity of a crystalline calcium salt. On washing this salt, decomposing it with hydrochloric acid, and extracting with ether, a solid acid is obtained which crystallises from chloroform in long, silky needles and melts at 84°. It is extremely soluble in water, ether, or ethyl acetate, but only sparingly so in benzene, and is almost insoluble in light petroleum.

0·1607 gave 0·2618 CO_2 and 0·0931 H_2O. C = 44·4 ; H = 6·3.
$C_7H_{12}O_6$ requires C = 43·8 ; H = 6·3 per cent.

The *silver* salt, $C_7H_8O_5Ag_2$, is precipitated as a white, crystalline powder on adding silver nitrate to a neutral solution of the ammonium salt. It explodes when heated. Analysis shows that it is the silver salt of the ketonic acid, $CO_2Ag\cdot CO\cdot CMe_2\cdot CH_2\cdot CO_2Ag$.

0·2516 gave 0·1395 Ag. Ag = 55·44.
$C_7H_8O_5Ag_2$ requires Ag = 55·6 per cent.
$C_7H_{10}O_6Ag_2$ „ Ag = 53·2 „

The *calcium* salt, $C_7H_{10}O_6Ca$, is characteristic, and separates slowly in the form of needles from a slightly alkaline solution of the ammonium salt on the addition of calcium chloride.

Condensation Product with o-Tolylenediamine,

$$CO_2H\cdot CH_2\cdot CMe_2\cdot C(:N\cdot C_6H_3\cdot CH_3)\cdot CO\cdot NH$$

—When a clear solution of *o*-tolylenediamine hydrochloride was mixed with sodium acetate and added to an aqueous solution of the acid and the whole boiled for a few minutes and allowed to stand, a crystalline precipitate separated which, after recrystallising from water, gave the following results on analysis:

0·2013 gave 0·4772 CO_2 and 0·1135 H_2O. C = 64·6; H = 6·3.
0·1582 ,, 0·3755 CO_2 ,, 0·0895 H_2O. C = 64·7; H = 6·3.
0·1810 ,, 17·2 c.c. nitrogen at 21° and 770 mm. N = 10·96.
$C_{14}H_{16}O_3N_2$ requires C = 64·6; H = 6·1; N = 10·8 per cent.

There can scarcely be a doubt that the constitution of this condensation product is that represented by the formula given above, and it is quite possible that other *α*-ketonic acids will be found to react with *o*-tolylenediamine and other *o*-diamines in the same way, yielding condensation products which may prove valuable as a means of diagnosing the nature of such acids.

Lactone of α-Hydroxy-ββ-dimethylglutaric Acid,

$$CH_2\cdot CMe_2\cdot CH(CO_2H)\cdot CO\cdot O$$

In preparing this lactone, 5 grams of pure dihydroxydimethylglutaric acid (see previous section) were dissolved in sodium carbonate solution, and treated with excess of sodium amalgam in the cold; a stream of carbon dioxide being led into the solution during the process. After standing overnight, the solution was evaporated to a small bulk, acidified, and repeatedly extracted with ether, when on evaporating off the ether a solid substance remained, which was purified by treating the solution in water with excess of ammonia, evaporating to dryness, and extracting the well dried solid ammonium salt with absolute alcohol. The alcoholic solution after filtering and mixing with four times its bulk of dry ether, gradually deposited small prisms of an ammonium salt, which were collected, decomposed with dilute hydrochloric acid, and the solution extracted with ether. The solid lactone which remained after distilling off the ether was readily crystallised from a small quantity of water, from which it separated in glistening prisms, and these, after standing on a piece of porous plate exposed to the air for a week, furnished the following numbers on analysis:

0·0988 gave 0·1740 CO_2 and 0·0614 H_2O. C = 48·0; H = 6·9.
$C_7H_{10}O_4,H_2O$ requires C = 47·8; H = 6·8 per cent.

This substance, which consists therefore of the lactone crystallising

with 1 mol. of water, melts indefinitely between 50° and 80°, at the same time giving up its water of crystallisation. In a vacuum desiccator over sulphuric acid, the hydrated crystals soon become opaque owing to loss of water, and the dehydrated substance then melts at 112° and consists of the pure lactone of α-hydroxydimethylglutaric acid.

0·1586 gave 0·3103 CO_2 and 0·0909 H_2O. C = 53·3 ; H = 6·4.
$C_7H_{10}O_4$ requires C = 53·2 ; H = 6·3 per cent.

This lactone is identical in all its properties with the lactone prepared by us (Trans., 1899, **75**, 56) by the action of sodium carbonate on ethyl hydrogen α-bromo-ββ-dimethylglutarate,

$$CO_2H\cdot CHBr\cdot CMe_2\cdot CH_2\cdot CO_2H,$$

but at that time it was not noticed that the lactone possessed the property of crystallising with water.

The rather remarkable property of a lactone crystallising with water without being converted into the hydroxy-acid has been observed before. Thus, Baeyer and Villiger (*Ber.*, 1897, **30**, 1955) showed that the β-lactone of dimethylmalic acid crystallises in prisms of the formula $C_6H_8O_4,H_2O$, and, as other examples, terpenylic acid and the lactones of hydroxycamphoronic acid, all of which crystallise with water, may be cited.

Action of Ethyl Alcoholic Potash on Ethyl αα₁-Dibromo-ββ-dimethylglutarate. Formation of Ethoxycaronic Acid, $Me_2C<\begin{matrix}C(OEt)\cdot CO_2H\\ CH\cdot CO_2H\end{matrix}$.

The action of alcoholic potash on this dibromo-ester was studied with the view of preparing an acid of the formula $Me_2C<\begin{matrix}C\cdot CO_2H\\ \|\\ C\cdot CO_2H\end{matrix}$ the ethyl ester of which, as stated in the introduction, we considered to be an intermediate product in the formation of the yellow sodium compound (p. 732). We were, however, unable to obtain this unsaturated acid by this reaction, owing to the readiness with which it adds on alcohol to form ethoxycaronic acid.

The hydrolysis was accomplished by heating equal weights of the bromo-ester and potash (dissolved in ethyl alcohol) for 3 hours on the water-bath, and then evaporating off the alcohol. The residue was dissolved in water, acidified, and extracted with ether in the usual way. The semi-solid mass which remained after distilling off the ether, yields a crystalline acid on rubbing with concentrated hydrochloric acid ; this was collected and purified by crystallisation from benzene.

0·1871 gave 0·3662 CO_2 and 0·1174 H_2O. C = 53·4; H = 7·0.
0·1659 „ 0·3255 CO_2 „ 0·1036 H_2O. C = 53·5; H = 7·0.
$C_9H_{14}O_5$ requires C = 53·4; H = 6·9 per cent.

Ethoxycaronic acid crystallises from benzene or water in long needles and melts at 138°; it is readily soluble in water, alcohol, or hot benzene, but only sparingly so in light petroleum.

One of its most characteristic salts is the *calcium* salt, which separates as a sparingly soluble crystalline precipitate on heating a neutral solution of the ammonium salt with calcium chloride.

The *silver* salt, $C_9H_{12}O_5Ag_2$, separates from a neutral solution of the ammonium salt on the addition of silver nitrate as a white, amorphous precipitate.

0·3195 gave 0·1652 Ag. Ag = 51·7.
$C_9H_{12}O_5Ag_2$ requires Ag = 51·8 per cent.

Ethoxycaronic Anhydride, $Me_2C\begin{<}{C(OEt)\cdot CO \atop CH\text{——}CO}\end{>}O$, is formed either when the acid is distilled under the ordinary pressure, or better, when it is heated with acetic anhydride and the product distilled.

It is a colourless oil which distils at 160—165° under 50 mm. pressure, and on boiling with water is again converted into ethoxycaronic acid.

0·1860 gave 0·3988 CO_2 and 0·1107 H_2O. C = 58·5; H = 6·6.
$C_9H_{12}O_4$ requires C = 58·6; H = 6·5 per cent.

Action of Sodium Ethoxide on Ethyl $\alpha\alpha_1$*-Dibromodimethylglutarate.*

Formation of Ethyl Ethoxycaronate, $Me_2C\begin{<}{C(OEt)\cdot CO_2Et \atop CH\cdot CO_2Et}\end{>}$.

This reaction was studied in order to show that the first action of sodium ethoxide on the dibromo-ester is to eliminate 2 mols. of hydrogen bromide, forming an unsaturated ester, $Me_2C\begin{<}{C\cdot CO_2Et \atop C\cdot CO_2Et}\end{>}$, which then either reacts with the alcohol present to form ethyl ethoxycaronate, or condenses with any other suitable substance, such as ethyl malonate, which may be present in the solution (p. 732).

Ethyl $\alpha\alpha_1$-dibromodimethylglutarate was digested with the theoretical quantity of sodium dissolved in alcohol, and the mixture heated on the water-bath until neutral. Water was then added, and the oil which separated, extracted with ether and fractionated under diminished pressure, when almost the whole quantity distilled at 160° under 35 mm. pressure as a colourless oil.

0·1866 gave 0·4055 CO_2 and 0·1412 H_2O. C = 59·3; H = 8 4.
$C_{13}H_{22}O_5$ requires C = 60·5; H = 8·5 per cent.

The rather low figures are accounted for by the fact that the substance contained a trace of bromine. That it was ethyl ethoxycaronate was proved by its behaviour on hydrolysis. The oil was heated for 2 hours with an equal weight of potash dissolved in alcohol, the alcohol removed by evaporation, and the residue acidified and extracted with ether, when on distilling off the ether a gum was obtained which gradually solidified. After crystallising twice from benzene, long colourless needles were obtained, which melted at 138° and consisted of pure *ethoxycaronic acid.*

0·1807 gave 0·3536 CO_2 and 0·1127 H_2O. C = 53·4 ; H = 6·9.
$C_9H_{14}O_5$ requires C = 53·5 ; H = 6·9 per cent.

The yield of ethyl ethoxycaronate obtained in the above experiment was 90 per cent. of the theoretical, and this method, therefore, affords a convenient way of obtaining this ester in quantity.

In the hope of being able to split off alcohol from ethyl ethoxycaronate, and then obtain the unsaturated ester, $Me_2C<\begin{matrix}C\cdot CO_2Et\\ \|\\ C\cdot CO_2Et\end{matrix}$, a quantity of the pure ester was heated to boiling for an hour under the ordinary pressure in a small distillation flask inclined so as to allow the oily liquid of high boiling point to flow back. On subsequent distillation, the whole passed over at 240°, and proved to be the unchanged ester.

0·1489 gave 0·3309 CO_2 and 0·1155 H_2O. C = 60·6 ; H = 8·6.
$C_{13}H_{22}O_5$ requires C = 60·5 ; H = 8·5 per cent.

Methoxycaronic Acid, $Me_2C<\begin{matrix}C(OMe)\cdot CO_2H\\ |\\ CH\cdot CO_2H\end{matrix}$.

When ethyl $\alpha\alpha_1$-dibromodimethylglutarate is digested with an equal weight of potash dissolved in methyl alcohol for 2 hours, it is completely hydrolysed and on evaporating, acidifying, and extracting with ether, a semi-solid mass is obtained which, when rubbed with cold hydrochloric acid, yields a quantity of crystals of methoxycaronic acid. These were collected and recrystallised from dilute hydrochloric acid, from which the substance separates in small prisms.

0·1867 gave 0·3507 CO_2 and 0·1081 H_2O. C = 51·2 ; H = 6·4.
$C_8H_{12}O_5$ requires C = 51·1 ; H = 6·4 per cent.

Methoxycaronic acid melts at 148°, and, when distilled, water is eliminated, and the acid converted into the *anhydride*, a colourless liquid boiling at 169° under 33 mm. pressure.

0·2164 gave 0·4821 CO_2 and 0·1149 H_2O. C = 56·7 ; H = 5·9.
$C_8H_{10}O_4$ requires C = 56·5 ; H = 5·9 per cent.

On boiling this anhydride with water, it is slowly reconverted into methoxycaronic acid.

Action of Sulphuric Acid and of Hydrobromic Acid on Ethoxy- and Methoxy-caronic Acids. Formation of αα-Dimethylsuccinic Acid, $CO_2H\cdot CMe_2\cdot CH_2\cdot CO_2H$, *and of αα-Dihydroxy-ββ-dimethylglutaric Acid,* $CO_2H\cdot C(OH)_2\cdot CMe_2\cdot CH_2\cdot CO_2H$.

When ethoxycaronic acid or methoxycaronic acid is heated with concentrated sulphuric acid at 100°, a rapid evolution of carbon monoxide ensues, and the liquid now contains *αα*-dimethylsuccinic acid, a curious decomposition, for which an explanation is given in the introduction. After the evolution of gas had ceased, the product was cooled, mixed with twice its volume of water, saturated with ammonium sulphate, and extracted several times with ether. The ethereal solution was dried and evaporated, when a solid acid was obtained which crystallised from hydrochloric acid in needles melting at 139—140°, and showed all the properties of *αα-dimethylsuccinic acid.*

0·1795 gave 0·3242 CO_2 and 0·1111 H_2O. C = 49·2; H = 6·9.
$C_6H_{10}O_4$ requires C = 49·3; H = 6·8 per cent.

The solution of this acid in a slight excess of ammonia gave, on boiling with calcium chloride, the characteristic calcium salt of dimethylsuccinic acid; and a quantity of the acid, after boiling with acetyl chloride and distillation, yielded the anhydride of dimethylsuccinic acid melting at 29°.

When either ethoxy- or methoxy-caronic acid is heated with concentrated hydrobromic acid in a sealed tube at 100° for 5 hours, it is quantitatively converted into *αα*-dimethylsuccinic acid.

If, however, the action of hydrobromic acid is first allowed to take place in the cold, that is to say, if the mixture of the ethoxy- or methoxy-acid and hydrobromic acid (saturated at 0°) is allowed to stand for 12 hours at the ordinary temperature and then evaporated on the water-bath, the product consists of an unstable bromo-acid which is evidently *αα*-dibromodimethylglutaric acid,

$$CO_2H\cdot CBr_2\cdot CMe_2\cdot CH_2\cdot CO_2H,$$

since on boiling with water it is quantitatively converted into *αα*-dihydroxydimethylglutaric acid, $CO_2H\cdot C(OH)_2\cdot CMe_2\cdot CH_2\cdot CO_2H$.

The acid thus obtained crystallised from chloroform in needles melting at 84° and a direct comparison showed that it was identical with the dihydroxy-acid prepared by the action of sodium carbonate on ethyl hydrogen *αα*-dibromodimethylglutarate, and described on p. 757.

0·1577 gave 0·2541 CO_2 and 0·0920 H_2O. C = 43·9 ; H = 6·4.
0·1713 „ 0·2751 CO_2 „ 0·0991 H_2O. C = 43·8 ; H = 6·4.
$C_7H_{12}O_6$ requires C = 43·8 ; H = 6·2 per cent.

Action of Ethyl Dibromodimethylglutarate on Ethyl Sodiomalonate. Formation of Ethyl Dicarboxydimethyltrimethylenemalonate,

$$Me_2C\begin{<}C(CO_2Et)\cdot CH(CO_2Et)_2\\ CH\cdot CO_2Et\end{<}.$$

For reasons explained in the introduction, and in order that this process, which lies at the base of the formation of the di*cyclo*pentane compounds described in this paper, should be thoroughly understood, the reaction was carried out under varied conditions, two of which may be described in detail.

Experiment I.—The proportions used were : ethyl malonate (2 mols.), sodium (2 at.), and ethyl dibromodimethylglutarate (1 mol.). The sodium (5 grams) was dissolved in 60 grams of absolute alcohol, mixed when nearly cold with the ethyl malonate (36 grams), and then with the dibromo-ester (40 grams). On heating the mixture on the water-bath, sodium bromide soon began to separate, and at the end of an hour the reaction was finished. The deep yellow product was washed with water and with dilute sodium carbonate, dried over calcium chloride, and evaporated, when 62 grams of an oil containing only traces of bromine were obtained. On distilling this under 30 mm. pressure, about 20 grams passed over below 135°, and consisted principally of ethyl malonate. The thermometer then rose rapidly to 215°, almost the whole of the residue passing over between this and 230°. Some of this fraction was redistilled, and the portion boiling at 222° under 30 mm. pressure analysed.

0·1511 gave 0·3191 CO_2 and 0·1055 H_2O. C = 57·6 ; H = 7·7.
$C_{18}H_{28}O_8$ requires C = 58·0 ; H = 7·5 per cent.

This ester gave, on hydrolysis, the lactones of the hydroxydimethylbutanetricarboxylic acids (p. 764), and when treated with sodium ethoxide and ethyl iodide it was converted into ethyl dicarboxyethyldimethyltrimethylenemalonate (p. 770) ; there can therefore be no doubt that it is *ethyl dicarboxydimethyltrimethylenemalonate*, and has the constitution represented by the formula at the head of this section.

Experiment II.—The proportions used were approximately 21 grams of ethyl malonate (1 mol.), 6 grams of sodium (2 at.), and 47 grams of ethyl dibromodimethylglutarate (1 mol.). The details of the carrying out of the reaction and isolation of the product were the same as in Expt. I. The 45 grams of neutral oily product obtained distilled, for

the most part, at 222—225° under 30 mm. pressure, and furnished the following results on analysis :

0·1366 gave 0·288 CO_2 and 0·0952 H_2O. C = 57·7 ; H = 7·7.
$C_{18}H_{28}O_8$ requires C = 58·0 ; H = 7·5 per cent.

A small quantity of this oil, on hydrolysis, yielded the same products as in the case of the ester obtained in Expt. I, so that it also must be *ethyl dicarboxydimethyltrimethylenemalonate.*

Hydrolysis of Ethyl Dicarboxyldimethyltrimethylenemalonate. Formation of the Lactones of A- and B-Hydroxydimethylbutanetricarboxylic Acids, $Me_2C<\begin{matrix}C(CO_2H)\cdot CH_2\cdot CO_2H\\ CH_2\cdot CO\cdot O\end{matrix}$, and

$$Me_2C<\begin{matrix}CH(CH_2\cdot CO_2H)\\ CH(CO_2H)\text{—}O\end{matrix}>CO.$$

When equal weights of the ethyl ester and potash are dissolved in methyl alcohol, a deep yellow solution is formed, which, on heating, gradually loses its yellow colour, and is completely hydrolysed after boiling for 2 hours. Water is now added, and the solution, after evaporating until quite free from methyl alcohol, and then acidifying, is saturated with ammonium sulphate and extracted at least 20 times with ether. The ethereal solution, after drying over calcium chloride and evaporating, deposits a thick, brown oil, which on standing becomes semi-solid ; in contact with porous porcelain, most of the oily matter is absorbed in about a week, leaving a brown, crystalline mass weighing about one-third of the ester employed in the hydrolysis. When this crude mass is ground up with cold water, about half dissolves, and on filtering on the pump an ochre-coloured substance remains, which is sparingly soluble in cold water, and may be readily obtained in the form of colourless prisms by repeated recrystallisation from water with the aid of animal charcoal.

0·1376 gave 0·2522 CO_2 and 0·0698 H_2O. C = 50·0 ; H = 5·6.
0·1730 „ 0·3168 CO_2 „ 0·0884 H_2O. C = 49·9 ; H = 5·7.
$C_9H_{12}O_6$ requires C = 50·0 ; H = 5·6.

This *lactone* of *B-hydroxydimethylbutanetricarboxylic acid* melts, when rapidly heated, at about 188—190° with evolution of gas, but the melting point, which is in reality the decomposing point, varies considerably with the rate of heating.

That this substance is a dibasic acid is proved by its behaviour on titration with decinormal caustic soda, when 0·2635 gram required for neutralisation 0·1 gram NaOH. Assuming the acid to be dibasic, this quantity should have neutralised 0·098 gram NaOH ; boiling with

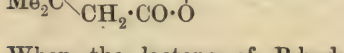
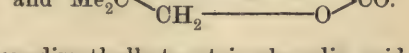
excess of decinormal soda appears to hydrolyse the lactone ring only very gradually.

The *Lactone of A-Hydroxydimethylbutanetricarboxylic Acid.*—The aqueous solution obtained by treating the crude solid product of the hydrolysis of the ester with cold water, as described above, was saturated with hydrogen chloride, taking care that the temperature did not rise above 40° during the operation. After standing for some days, the crystals which had separated were collected, washed with hydrochloric acid, * dissolved in as little water at 50° as possible, and the solution cooled with ice and well stirred, when a very small quantity of the lactone of the B-acid crystallised out. After filtering, the filtrate was saturated with hydrogen chloride as before, and the crystals, which separated on standing, were collected, drained on porous porcelain, dried at 80°, and analysed :

0·1581 gave 0·2836 CO_2 and 0·0819 H_2O. C = 48·9 ; H = 5·7.
0·1423 ,, 0·2586 CO_2 ,, 0·0737 H_2O. C = 49·5 ; H = 5·7.
$C_9H_{12}O_6$ requires C = 50·0 ; H = 5·6 per cent.

This lactone, when heated in a capillary tube, decomposes with evolution of gas at about 158° ; it is much more readily soluble in water than the lactone of the B-hydroxy-acid. On titration, it behaves as a dibasic acid, since 0·2398 gram required for neutralisation 0·088 gram NaOH, whereas this amount of a dibasic acid, $C_9H_{12}O_6$, should neutralise 0·086 gram NaOH.

Lactones of A- and B-Hydroxydimethylbutanedicarboxylic Acids,


and


When the lactone of B-hydroxydimethylbutanetricarboxylic acid (m. p. 188°) is heated at 190—200°, it decomposes with evolution of carbon dioxide, and in investigating this curious decomposition, we, in the first place, determined quantitatively the amount of gas produced in this way. The experiment was carried out by heating the substance to its decomposing point in a platinum boat in an empty piece of combustion tube, placed in a combustion furnace, and collecting the carbon dioxide evolved in potash bulbs, much in the same way as if an elementary analysis were being performed.

I. 0·577 gave 0·1098 CO_2. CO_2 = 19·0.
II. 0·453 ,, 0·0937 CO_2. CO_2 = 20·7.

* The mother liquors from these crystals, on evaporation at the ordinary temperature over sulphuric acid and solid potash in a vacuum desiccator, deposit a further crop of crystals of the same substance.

Assuming the reaction $C_9H_{12}O_6 = C_8H_{12}O_4 + CO_2$ to take place, the loss of carbon dioxide should be 20·4 per cent.

A portion of the residue in experiment II, after boiling with water and animal charcoal and evaporating to dryness, was analysed, with the following results:

0·113 gave 0·232 CO_2 and 0·0712 H_2O. C = 56·0; H = 6·7.

$C_8H_{12}O_4$ requires C = 55·8; H = 7·0 per cent.

so that, apparently, no decomposition other than loss of carbon dioxide takes place during this process.

About 5 grams of the pure lactone of the B-hydroxytribasic acid were now heated at 200° in a test-tube, placed in a sulphuric acid bath until all evolution of gas had ceased, and the residue, which was a thick, almost colourless, resin very readily soluble in water, was dissolved in a slight excess of dilute ammonia, and the solution mixed with calcium chloride. The crystalline, sparingly soluble calcium salt, which gradually separated on boiling, was collected on the pump, rapidly washed with hot water, decomposed with dilute hydrochloric acid and the solution repeatedly extracted with pure ether. After drying over calcium chloride and evaporating off the ether, a thick, transparent resin remained which, on standing for some weeks in a desiccator over sulphuric acid, began to crystallise in nodular masses and ultimately became quite hard. On grinding up the mass with hydrochloric acid, a trace of oily impurity was removed and the residue, after draining on porous porcelain, was a hard, colourless, crystalline substance which melted at 107—108°, and was analysed with the following results:

0·1256 gave 0·2538 CO_2 and 0·0772 H_2O. C = 55·1; H = 6·8.

$C_8H_{12}O_4$ requires C = 55·8; H = 7·0 per cent.

As these numbers were rather low, the substance was dissolved in a very little water, the solution saturated with hydrogen chloride at about 30° and allowed to stand, when hard, crystalline crusts separated, which, however, furnished a still less satisfactory result on analysis:

0·1571 gave 0·3152 CO_2 and 0·0950 H_2O. C = 54·7; H = 6·7 per cent.

It was then found that the crystals, which again melted at 108°, contained traces of chlorine, due, no doubt, to the action of the hydrochloric acid, and this accounts for the rather low analytical numbers.

The *lactone* of *B-hydroxydimethylbutanedicarboxylic acid* is very readily soluble in water, forming a strongly acid solution, which on titration takes up rather more alkali than calculated on the basis of its being a monobasic acid, showing that hydrolysis of the lactone ring takes place to a small extent at the ordinary temperature.

0·2064 gram of the acid dissolved in cold water required for neutral-

isation 0·054 gram NaOH, whereas this quantity of a monobasic acid, $C_8H_{12}O_4$, requires 0·048 gram NaOH, but if it became dibasic in solution it would neutralise 0·096 gram NaOH.

The *calcium* salt, $(C_8H_{11}O_4)_2Ca,4H_2O$ (?), obtained as described above, and dried at 100°, was analysed:

0·2300 gave 0·1026 $CaSO_4$. Ca = 13·1 per cent.

A different sample of the salt was prepared from the acid melting at 108° by boiling with excess of calcium chloride and ammonia. The crystalline crusts which separated were well washed with hot water, dried at 100°, and analysed, with the same result as before:

0·1303 gave 0·057 $CaSO_4$. Ca = 13·2 per cent.

These numbers agree well with the formula $(C_8H_{11}O_4)_2Ca,4H_2O$, which requires Ca = 13·3 per cent., but this formula must remain doubtful until an actual determination of the water of crystallisation has been made. It is, however, worthy of note that other calcium salts of similarly constituted lactonic acids are known which contain water of crystallisation, and do not become anhydrous at 100°. Thus, for example, the calcium salt of the lactone of α-hydroxydimethyltricarballylic acid (Baeyer, *Ber.*, 1896, **29**, 2795) has the formula $C_8H_8O_6Ca,3H_2O$, and still contains 1 mol. of water of crystallisation when dried at 125° until constant.

When the lactone of A-hydroxydimethylbutanetricarboxylic acid, (m. p. 158°) is heated at 200°, it is decomposed like the lactone of the B-acid with elimination of carbon dioxide and formation of a resinous substance very soluble in water. As it was thought at the time that this was probably the same acid (m. p. 108°) as that obtained from the lactone of the B-hydroxy-acid, the whole was boiled with excess of ammonia and calcium chloride, but no crystalline salt separated until the solution had been evaporated to a small bulk, and this on cooling and diluting with a little water again dissolved completely.

The whole was acidified and extracted with ether, and the residue, after distilling off the ether, allowed to stand over sulphuric acid, when it gradually became semi-solid. After 10 days, the mass was ground up in a mortar with concentrated hydrochloric acid, which dissolved the resinous impurity, and left a colourless, crystalline acid; this, after washing with hydrochloric acid, melted at 154—156°, with slight previous softening, and furnished the following numbers on analysis:

0·157 gave 0·3186 CO_2 and 0·0947 H_2O. C = 55·3; H = 6·7.

$C_8H_{12}O_4$ requires C = 55·8; H = 7·0 per cent.

The *lactone* of *A-hydroxydimethylbutanedicarboxylic acid* is much less soluble in water than that of the B-acid. That it is a monobasic lactonic acid is shown by the following results, which were obtained on titration with decinormal caustic soda.

0·145 gram dissolved in hot water and the solution, after cooling to 20°, titrated rapidly, neutralised 0·043 gram NaOH; on adding excess of decinormal caustic soda, boiling for a few minutes, and titrating back, it was found that 0·064 gram NaOH had been taken up. This amount of a monobasic acid, $C_8H_{12}O_4$, requires 0·034 gram NaOH, and if dibasic 0·067 gram NaOH, for neutralisation.

These numbers show, therefore, that the acid is a monobasic lactone acid, but, that in aqueous solution, partial hydrolysis of the lactone ring has taken place, such hydrolysis to the disbasic hydroxy-acid being complete when the solution is boiled with an excess of decinormal caustic soda.

Action of Sodium Ethoxide on Ethyl Dicarboxydimethyltrimethylenemalonate. Formation of the Yellow Sodium Compound of Ethyl Dimethylketodicyclopentanetricarboxylate,

$$Me_2C\begin{cases}C(CO_2Et)\cdot CNa\cdot CO_2Et\\ C(CO_2Et)\cdot CO\end{cases}.$$

This interesting condensation was carried out in alcoholic solution with sodium ethoxide and also in xylene solution by the action of sodium, in both cases with the same result, so that the first experiment only need be described in detail.

The pure ethyl ester (5 grams) was dissolved in alcohol, mixed with an excess of a strong solution of sodium ethoxide containing 2 grams of sodium, and heated on the water-bath for 3 hours. The deep yellow solution was then evaporated to remove alcohol as far as possible, and mixed with water, when a quantity of the yellow sodium compound separated, and this, after washing first with water and then with alcohol and ether and drying at 100°, was analysed, with the following result:

0·3512 gave 0·0727 Na_2SO_4. Na = 6·7.

$C_{16}H_{21}O_7Na$ requires Na = 6·6 per cent.

This yellow sodium compound when dissolved in methyl alcohol gave an intense red coloration with ferric chloride, and on hydrolysis with dilute sulphuric acid was converted into *dimethylketodicyclopentanecarboxylic acid* melting at 180°; therefore there can be no doubt that it is identical with the yellow sodium compound which was subsequently prepared in large quantities by the process explained on p. 776.

On acidifying the mother liquor from which the sodium compound had been isolated as described above, an oil separated which, when hydrolysed with dilute sulphuric acid, gave a considerable quantity of the above ketonic acid melting at 180°. This oil, which is evidently an acid ethyl ester, is doubtless the same as that always produced in the preparation of the yellow sodium compound by the process given on p. 776.

Ethyl Dicarboxydimethyltrimethylenebromomalonate,

$$Me_2C<\begin{matrix}C(CO_2Et)\cdot CBr(CO_2Et)_2\\ CH\cdot CO_2Et\end{matrix},$$

When ethyl dicarboxydimethyltrimethylenemalonate (11 grams) was mixed with rather more than the theoretical quantity of bromine (5 grams) and the mixture heated on the water-bath in a flask fitted with a long air condenser, hydrogen bromide was evolved in quantity, and after 3 hours the whole of the bromine had disappeared. The product was poured into water, extracted with ether, the ethereal solution washed repeatedly with dilute sodium carbonate, dried over calcium chloride, and evaporated, when a heavy, brown oil was obtained which, after standing for some days over sulphuric acid in a vacuum, furnished the following results on analysis:

0·4342 gave 0·1863 AgBr. Br = 18·3.

$C_{18}H_{27}O_8Br$ requires Br = 17·7 per cent.

Hydrolysis with Alcoholic Potash.—When this bromo-ester was mixed with excess of alcoholic potash, hydrolysis took place readily, and after heating on the water-bath for 2 hours water was added, the clear liquid evaporated to dryness, acidified, and repeatedly extracted with ether.

The gum which remained after distilling off the ether was dissolved in a slight excess of ammonia and boiled with calcium chloride, by which means a considerable quantity of coloured impurity was precipitated.

After filtering, the filtrate was acidified, again extracted with ether, and the gummy acid heated at 200° until evolution of gas ceased; the dark coloured mass was then ground up with pure dry ether, which dissolved the oily impurity and left a small quantity of a sandy, crystalline powder. This was dissolved in much dry ether, the ethereal solution evaporated to a small bulk and allowed to stand, and the crystalline crust, which gradually separated, collected and analysed:

0·1214 gave 0·2425 CO_2 and 0·0554 H_2O. C = 54·5; H = 5·1.

$C_9H_{10}O_5$ requires C = 54·5; H = 5·1 per cent.

As explained in the introduction, it is exceedingly probable that this substance is

Anhydrodimethyltetramethylenetricarboxylic Acid,

$$Me_2C<\begin{matrix}CH(CO_2H)\cdot CH\cdot CO\\ \text{———————}\\ CH\cdot CO\end{matrix}>O.$$

It melts at 207—210° and is very sparingly soluble in ether or light petroleum, but readily soluble in acetone; it dissolves readily in water on boiling, forming a very soluble acid, which, on evaporating the solution almost to dryness, is obtained in the form of crystals, but owing to the difficulty of purifying it, has not yet been isolated in a form suitable for analysis.

That a tribasic acid is formed in this way is proved by the following experiment. 0·0684 gram of the pure anhydro-acid was boiled with water and the solution titrated with decinormal sodium hydroxide, when 0·0416 gram NaOH were neutralised; assuming that the acid formed is tribasic, this amount should neutralise 0·0415 gram NaOH.

The solution thus obtained is stable to permanganate for several minutes, showing that the acid is saturated.

Ethyl Dicarboxydimethyltrimethylene-ethylmalonate,

$$Me_2C<\begin{matrix}C(CO_2Et)\cdot CEt(CO_2Et)_2\\ |\\ CH\cdot CO_2Et\end{matrix}.$$

In preparing this ester, ethyl dicarboxydimethyltrimethylenemalonate (11 grams) was added to a solution of sodium (0·9 gram) in absolute alcohol (15 grams) and the yellow solution then mixed with ethyl iodide (10 grams) and heated for 6 hours on the water-bath. The oil, which was precipitated on adding water, was extracted with ether, the ethereal solution well washed with water, dried over calcium chloride, and evaporated, and the residual yellow oil fractionated, when almost the whole quantity passed over at 230—232° under 30 mm. pressure as a slightly yellow oil, which was analysed with the following results:

0·1633 gave 0·3516 CO_2 and 0·1141 H_2O. C = 58·7; H = 7·7.
$C_{20}H_{32}O_8$ requires C = 60·0; H = 8·0 per cent.

As the results of analysis seemed to indicate that the substance might still contain some of the original ester, which had escaped the action of the sodium ethoxide and ethyl iodide, it was treated again, exactly as before, with these reagents. The product, which distilled at the same temperature as before, now furnished correct results on analysis:

0·1754 gave 0·3871 CO_2 and 0·1239 H_2O. C = 60·2; H = 7·8.
0·1403 ,, 0·3088 CO_2 ,, 0·1019 H_2O. C = 60·0; H = 8·1.
$C_{20}H_{32}O_8$ requires C = 60·0; H = 8·0 per cent.

Ethyl dicarboxydimethyltrimethylene-ethylmalonate, which is formed almost quantitatively in the above reaction, is a thick oil which, when heated in small quantities, appears to distil under the ordinary pressure, almost without decomposition.

Dimethylethylethoxyketopentamethylenedicarboxylic Acid,

$$Me_2C\begin{cases}C(OEt)(CO_2H)\cdot CEt\cdot CO_2H\\ CH_2\text{———}CO\end{cases}$$

This substance is produced by the hydrolysis of the ester described in the previous section. The pure ester (20 grams) was added to a solution of potash (25 grams) in methyl alcohol, when a dark yellow solution was produced which, on boiling, gradually became dark brown. After 2 hours water was added, the solution evaporated until free from alcohol, extracted with ether to remove a trace of neutral oil, acidified, and the liquid, after saturating with ammonium sulphate, extracted 20 times with ether; the ethereal solution was then dried over calcium chloride and evaporated. The dark-brown residue (12 grams) gradually deposited crystals, and after 10 days the semi-solid mass was well stirred with a little cold water, filtered on the pump, and the ochre-coloured residue (6 grams) dissolved in hot water, boiled with animal charcoal, and filtered. The filtrate on slowly cooling deposited beautiful, glistening, prismatic needles, which were collected, recrystallised from water, and analysed:

0·178 gave 0·3736 CO_2 and 0·1197 H_2O. C = 57·2; H = 7·5.

$C_{13}H_{20}O_6$ requires C = 57·3; H = 7·3 per cent.

The acid melts at 175° without decomposition, but gives off gas slowly at 190°, much more rapidly at 200—210°.

The *silver* salt, $C_{13}H_{18}O_6Ag_2$, was obtained as a white, crystalline powder on adding silver nitrate to a warm, slightly alkaline solution of the ammonium salt. On analysis:

0·2165 gave 0·2520 CO_2, 0·075 H_2O, and 0·0954 Ag.

C = 31·7; H = 3·8; Ag = 44·1.

$C_{13}H_{18}O_7Ag_2$ requires C = 32·1; H = 3·7; Ag = 44·3 per cent.

As this substance was at first thought to be an acid ester (see p. 748), experiments were tried as to its behaviour with strong alkalis, with the view of further hydrolysing it.

It was found, however, that digestion with aqueous potash or baryta apparently had no effect on it, as, on acidifying, the greater part of the substance was recovered unchanged. In one experiment, the substance was digested with a large excess of aqueous potash (10 per cent.) for 2 hours when, on acidifying and extracting with ether, a

solid was obtained which crystallised beautifully from water, and furnished the following numbers on analysis:

0·1628 gave 0·3462 CO_2 and 0·1071 H_2O. C = 57·9; H = 7·3.

$C_{13}H_{20}O_6$ requires C = 57·3; H = 7·3 per cent.

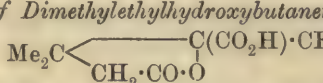
Since these crystals melted at 170—175°, it is evident that boiling with potash had not effected any change in the substance.

When the pure substance is heated in a fractionating flask, it decomposes and gives off a small quantity of a liquid of low boiling point which is apparently alcohol; the residue then distils at 270—300° with hardly any charring. On redistillation, almost the whole quantity passed over at 270—275° as a colourless oil which, on analysis, gave the following numbers:

0·1524 gave 0·3614 CO_2 and 0·1031 H_2O. C = 64·7; H = 7·5.

Unfortunately, the quantity of this oil at our disposal was too small to allow of further investigation.

Lactone of Dimethylethylhydroxybutanetetracarboxylic Acid,



The dark-coloured aqueous mother liquors obtained after the separation of the crystals of dimethylethylethoxyketopentamethylenedicarboxylic acid from the semi-solid product of the hydrolysis of ethyl dicarboxydimethyltrimethylene-ethylmalonate, as described in the last section, were boiled with an excess of barium hydroxide, and the almost colourless, bulky, amorphous precipitate which formed was collected on the pump and well washed with water.

The salt was then decomposed by dilute hydrochloric acid, the clear solution extracted 10 times with ether, the ethereal solution dried over calcium chloride and evaporated, when a transparent, resinous residue was obtained, which on rubbing with a glass rod gradually became semi-solid. The mass was left in contact with porous porcelain until dry, and purified by recrystallisation from warm water with the aid of animal charcoal. The substance separates from water in minute prisms, and under the microscope is seen to be quite homogeneous; it melts at about 193°, with evolution of gas.

0·178 gave 0·3275 CO_2 and 0·0906 H_2O. C = 50·1; H = 5·6.

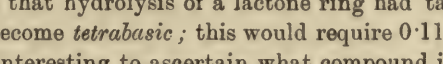
$C_{12}H_{16}O_8$ requires C = 50·0; H = 5·6 per cent.

That this substance is the *lactone* of *dimethylethylhydroxybutanetetracarboxylic acid*, and has the constitution represented at the head of this section, is rendered probable, not only by the analysis, but also by the results obtained on titration with decinormal sodium hydroxide.

0·2075 gram dissolved in cold water and rapidly titrated, required for neutralisation 0·084 gram NaOH, whereas this amount of a substance of the formula $C_{12}H_{16}O_8$, if *tribasic*, should neutralise 0·086 NaOH. On boiling with an excess of the alkali for a few minutes and titrating back, it was found that 0·115 gram of NaOH had now been neutralised, indicating that hydrolysis of a lactone ring had taken place, and the substance become *tetrabasic*; this would require 0·115 gram NaOH.

It would be interesting to ascertain what compound is formed when this substance decomposes at 193°, but unfortunately the small quantity of material at our disposal was insufficient for the purpose.

Lactone of trans-*Dimethylethylhydroxybutanetricarboxylic Acid*,



The dark brown aqueous filtrate from the insoluble barium salt described in the last section was acidified and repeatedly extracted with ether, when, on evaporation of the ether, a new acid was obtained which crystallised well from water in prismatic needles, and melted at about 213° without decomposition. This was analysed, with the following results:

0·1548 gave 0·3027 CO_2 and 0·0890 H_2O. C = 53·3; H = 6·4.

$C_{11}H_{16}O_6$ requires C = 54·1; H = 6·5 per cent.

During the combustion, it was noticed that a beautifully crystalline sublimate, probably of an anhydride, formed on the cooler portions of the tube. Although this substance has only been obtained in small quantities, it is probable that it is one of the stereoisomeric modifications of the *lactone* of *dimethylethylhydroxybutanetricarboxylic acid*, and as it melts at a higher temperature than the other modification (see next section) and is not, like the latter, converted into an anhydride at this temperature, we have named it the *trans*-modification.

That this substance is a dibasic lactonic acid is borne out by the results of the following titration with decinormal sodium hydroxide, which was carried out with the remaining small quantity of the material.

0·0522 gram required for neutralisation 0·0165 gram NaOH, whereas, if *dibasic*, it should have neutralised 0·0171 gram NaOH. On boiling with excess of alkali and titrating back, it was found that 0·024 gram NaOH had been neutralised, indicating that a lactone ring had been hydrolysed and the acid become *tribasic*; this would require 0·0256 gram NaOH.

Lactone of cis-*Dimethylethylhydroxybutanetricarboxylic Acid.*

This acid has been prepared in considerable quantity by the hydrolysis of dimethylethylethoxyketopentamethylenedicarboxylic acid with hydrochloric acid. The pure substance was boiled with concentrated hydrochloric acid in a reflux apparatus until the crystals had completely dissolved, which was the case after about six hours. On standing overnight, a small quantity of colourless, needle-shaped crystals had formed, and a further large quantity separated on vigorously shaking the liquid; these were collected and purified by crystallisation from water.

This new substance exhibits in a marked degree the tendency to form supersaturated solutions; when it crystallises moderately rapidly it is obtained in the form of needles, but when the separation is slow and extends over several days, it is deposited in hard prisms, somewhat resembling crystals of cane sugar.

These prisms gave the following results on analysis, showing that in this form the substance crystallises with water:

0·1522 gave 0·281 CO_2 and 0·0959 H_2O. C = 50·4; H = 7·0.
$C_{11}H_{16}O_6,H_2O$ requires C = 50·4; H = 6·9 per cent.

On the other hand, a specimen from a different preparation which had separated from hydrochloric acid in flat, glistening needles was evidently anhydrous.

0·14 gave 0·276 CO_2 and 0·0851 H_2O. C = 53·7; H = 6·7.
$C_{11}H_{16}O_6$ requires C = 54·1; H = 6·5 per cent.

The *lactone* of cis-*dimethylethylhydroxybutanetricarboxylic acid* has no definite melting point, since when heated in a capillary tube it decomposes, with evolution of gas, at temperatures ranging from about 144° in the case of the prisms to 153° in the case of the needles. It dissolves much more readily in water than the ethoxy-acid from which it was obtained, and on titration with decinormal sodium hydroxide it gives numbers which characterise it as a dibasic lactonic acid.

0·4478 gram of the prisms, dissolved in cold water, neutralised 0·147 gram NaOH, whereas this quantity of a *dibasic acid* of the formula $C_{11}H_{16}O_6,H_2O$ should neutralise 0·133 gram NaOH. This shows that on dissolving the substance in water partial hydrolysis of the lactone ring takes place. Excess of decinormal sodium hydroxide was now added, and after the liquid had been boiled for some time it was found, on titrating back, that 0·196 gram NaOH had been neutralised, whereas for the neutralisation of the *tribasic acid*, 0·192 gram should have been taken up.

Silver Salt, $C_{11}H_{15}O_7Ag_3$.—In preparing this salt, the acid was boiled with water and excess of ammonia, evaporated until nearly neutral, and precipitated with silver nitrate. The white, amorphous salt thus obtained gave numbers, on analysis, showing that it was the salt of the tribasic acid and not of the dibasic lactonic acid.

0·2412 gave 0·1317 Ag. Ag = 54·6.
$C_{11}H_{15}O_7Ag_3$ requires Ag = 55·1 per cent.

The tribasic *barium* salt, $(C_{11}H_{15}O_7)_2Ba_3$, is obtained on adding excess of boiling barium hydroxide solution to a hot aqueous solution of the lactonic acid, as a heavy, white precipitate, which was rapidly collected on the pump, washed with boiling water, dried at 100°, and analysed :

0·5421 gave 0·4083 $BaSO_4$. Ba = 44·3.
$C_{22}H_{30}O_{14}Ba_3$ requires Ba = 44·2 per cent.

Anhydride of the Lactone of cis-*Dimethylethylhydroxybutanetricarboxylic Acid*, $\begin{matrix} Me_2C \\ | \\ CH_2\cdot CO\cdot O \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} CO\text{—}O \\ | \\ CHEt\cdot CO \end{matrix}$.—If the acid is heated at 180° until the evolution of gas has ceased, and then allowed to solidify, its melting point will now be found to be 160—164°, a change which is due to the formation of the anhydride. This anhydride is easily obtained in a pure condition when the acid is heated for half an hour with excess of acetyl chloride and the solution evaporated to dryness. The solid residue is powdered, extracted with boiling light petroleum (b. p. 80—100°), which removes a trace of impurity but dissolves very little of the anhydride, and the residue is crystallised from benzene, from which it separates in lustrous plates. On analysis :

0·1701 gave 0·3638 CO_2 and 0·0981 H_2O. C = 58·3 ; H = 6·4.
$C_{11}H_{14}O_5$ requires C = 58·4 ; H = 6·2 per cent.

This anhydride melts at 168° and solidifies rapidly again at a few degrees below this temperature ; it is slowly hydrolysed by boiling water, and the solution, on evaporation over sulphuric acid, deposits colourless crystals decomposing at 144° and consisting of the original dibasic lactonic acid, no stereoisomeric change having taken place during the formation of the anhydride.

Experimental.

Part II. Preparation and Properties of the Yellow Sodium Compound of Ethyl 5:5-*Dimethyl*-3-*ketodi*cyclo*pentane*-1:2:4-*tricarboxylate and Description of the Acids obtained from it.*

By W. H. Perkin, jun., J. F. Thorpe, and C. Walker.

Condensation of Ethyl $\alpha\alpha_1$-*Dibromo*-$\beta\beta$-*dimethylglutarate with Ethyl Malonate in the Presence of Excess of Sodium Ethoxide. Preparation of the Sodium Compound of Ethyl Dimethylketodi*cyclo*pentane-tricarboxylate*, $Me_2C<\begin{matrix}C(CO_2Et)\cdot CNa\cdot CO_2Et\\ |\\ C(CO_2Et)\cdot CO\end{matrix}$.

This sodium compound, the formation of which by the action of sodium on ethyl dicarboxydimethyltrimethylenemalonate has been mentioned on p. 768, is best prepared in quantity by the following process.

Ethyl malonate (2 mols.) is mixed with a solution of sodium (4 at.) dissolved in alcohol, and then ethyl dibromodimethylglutarate (1 mol.) is gradually added. The mass at once assumes a deep yellow colour, which intensifies on heating on the water-bath, and if, after heating for 12 hours, the alcohol is distilled off and water added, a large yield of a yellow solid is precipitated; this can be separated by filtration and washed with water without undergoing change. The method usually adopted was to filter off the yellow sodium compound through a Buchner funnel on the pump, wash twice with water, then once with alcohol, and finally with dry ether, until all trace of oil had been removed.

For analysis, the yellow sodium compound was crystallised from boiling alcohol, from which it separates, on cooling, in lustrous yellow plates.

0·1790 gave 0·0370 Na_2SO_4. Na = 6·69.

$C_{16}H_{21}O_7Na$ requires Na = 6·60 per cent.

The yellow sodium compound prepared in this way is identical with that obtained by the method given on p. 768, where the principal properties of the substance are mentioned. The yield obtained by the above process is 60—65 per cent. of the theoretical.

From the ethereal and alcoholic washings of the sodium compound, a neutral and an acid portion can be extracted by shaking with sodium carbonate solution.

The neutral portion consists for the most part of unchanged ethyl malonate mixed with a small quantity of ethyl ethanetetracarboxylate, $(CO_2Et)_2CH\cdot CH(CO_2Et)_2$, melting at 76°.

The sodium carbonate solution, on acidifying, deposits a thick oil, which gives an intense red coloration with ferric chloride, and on hydrolysis with dilute sulphuric acid is converted into *dimethylketodicyclopentanecarboxylic acid* (p. 780).

Action of Cold Methyl Alcoholic Potash on the Yellow Sodium Compound. Formation of Diethyl Hydrogen Dimethylketodicyclopentanetricarboxylate and its Dipotassium Salt,

$$Me_2C<\begin{matrix}C(CO_2Et)\cdot CH\cdot CO_2Et\\ C(CO_2H)-CO\end{matrix} \quad \text{and} \quad Me_2C<\begin{matrix}C(CO_2Et)\cdot CK\cdot CO_2Et\\ C(CO_2K)-CO\end{matrix}.$$

When the yellow sodium compound is treated in the cold with an equal weight of potash dissolved in methyl alcohol, it passes into solution, and in a short time a large quantity of a *canary-yellow* potassium salt separates. This was collected on the pump, washed with methyl alcohol, and analysed, with the following result:

0·4878 gave 0·2066 K_2SO_4. K = 21·5.

$C_{14}H_{16}O_7K_2$ requires K = 21·0 per cent.

This potassium salt, which evidently has the constitutional formula represented above, is fairly soluble in cold water, and on acidifying the solution an oil is precipitated, which gradually sets to a solid mass of the corresponding diethyl hydrogen salt, a colourless substance which separates from dilute alcohol in long prisms and melts at 75°. On analysis:

0·1777 gave 0·3680 CO_2 and 0·0975 H_2O. C = 56·5; H = 6·1.

$C_{14}H_{18}O_7$ requires C = 56·4; H = 6·0 per cent.

This substance is very sparingly soluble in water, but readily so in sodium carbonate. Its alcoholic solution gives an intense purple coloration with ferric chloride.

B-Dimethylketodicyclopentanedicarboxylic Acid,

$$Me_2C<\begin{matrix}C(CO_2H)\cdot CH\cdot CO_2H\\ CH\text{———}CO\end{matrix}.$$

When the diethyl hydrogen salt, described in the last section, is heated under 30 mm. pressure, carbon dioxide is eliminated, and a thick oil distils over constantly at 210°, which gives in alcoholic solution, on the addition of ferric chloride, a rich purple coloration, and, as the analysis shows, consists of *ethyl dimethylketodicyclopentanedicarboxylate.*

0·2341 gave 0·5252 CO_2 and 0·1477 H_2O. C = 61·2; H = 7·0.

$C_{13}H_{18}O_5$ requires C = 61·4; H = 7·1 per cent.

On hydrolysing this ester with an equal weight of potash dissolved in alcohol, evaporating off the alcohol, acidifying with hydrochloric acid, and repeatedly extracting with ether, the corresponding acid is obtained as a solid, which crystallises from hydrochloric acid in long needles melting at 180°.

0·1568 gave 0·3073 CO_2 and 0·0750 H_2O. C = 53·6 ; H = 5·3.
0·1773 ,, 0·3530 CO_2 ,, 0·0813 H_2O. C = 54·3 ; H = 5·1.
$C_9H_{10}O_5$ requires C = 54·5 ; H = 5·1 per cent.

B-Dimethylketodicyclopentanedicarboxylic acid is very readily soluble in water, but much less so in hydrochloric acid ; its aqueous solution gives, with ferric chloride, a red coloration, and its solution in sodium carbonate is stable to permanganate for about 10 seconds.

The *silver* salt, $C_9H_8O_5Ag_2$, separates from a neutral solution of the ammonium salt, on the addition of silver nitrate, as a white, amorphous precipitate.

0·3145 gave 0·1642 Ag. Ag = 52·2.
$C_9H_8O_5Ag_2$ requires Ag = 52·3 per cent.

The *anhydride*, $C_9H_8O_3$, was prepared by boiling 2 grams of the acid with excess of acetic anhydride for 3 hours on the sand-bath, and then allowing the solution to evaporate over potash in a vacuous desiccator. The solid residue, which melted at about 150°, was dissolved in boiling light petroleum (b. p. 60—80°), filtered, and allowed to stand, when lustrous needles of the anhydride separated.

0·2134 gave 0·5134 CO_2 and 0·0928 H_2O. C = 65·6 ; H = 4·8.
$C_9H_8O_3$ requires C = 65·8 ; H = 4·8 per cent.

This substance melts at 152°, and is gradually dissolved by boiling water, being converted into the acid melting at 180°, from which it was derived.

On heating an aqueous solution of the acid at 180° for 6 hours, it was found to have been transformed into an acid sparingly soluble in water, and at the same time a considerable pressure was noticed on opening the tube. The acid thus produced crystallised from water in fern-like needles, melted at 180°, and was found to be identical with *dimethylketodicyclopentanecarboxylic acid* (p. 780) prepared by the action of dilute sulphuric acid on the sodium compound, and also by the action of heat on the A-modification of dimethylketodicyclopentanedicarboxylic acid (p. 779).

Action of Boiling Alcoholic Potash on the Yellow Sodium Compound. Formation of A- and B-Dimethylketodicyclopentanedicarboxylic Acids,

$$Me_2C<\begin{matrix}C(CO_2H)\cdot CH\cdot CO_2H\\ |\qquad\qquad |\\ CH\text{——}CO\end{matrix}.$$

When the yellow sodium compound (20 grams) is boiled with potash (16 grams) dissolved in alcohol, a copious precipitate of a *colourless* potassium salt separates from the clear solution after the heating has been continued for 2 hours. This potassium salt, which is very deliquescent, is rapidly collected on the pump, washed with absolute alcohol, dissolved in a little water, acidified, and repeatedly extracted with ether; the ethereal solution is then dried and evaporated, when a solid acid is obtained, which melts indefinitely between 140° and 170°. This solid is a mixture of the A- and B-modifications of dimethylketodi*cyclo*pentanedicarboxylic acid, and can be resolved into these by dissolving it in a small quantity of water and adding an equal volume of concentrated hydrochloric acid. On allowing the solution to stand, a crystalline acid slowly separates, consisting of the almost pure A-modification.

This acid is less soluble in water than the B-modification, and separates from dilute hydrochloric acid (1 : 1) in small prisms which melt at 153—155°, and undergo decomposition with evolution of carbon dioxide at 165°; its aqueous solution gives, with ferric chloride, an intense bluish-violet coloration.

0·1493 gave 0·2911 CO_2 and 0·0719 H_2O. C = 53·1; H = 5·3.
0·1738 ,, 0·3388 CO_2 ,, 0·0814 H_2O. C = 53·2; H = 5·2.
$C_9H_{10}O_5$ requires C = 54·5; H = 5·1 per cent.

These numbers are not so good as could have been wished, and this is apparently due to the acid containing a small quantity of the tribasic acid, directly derived from the yellow sodium compound.

That the acid has the constitution given to it at the head of this section is proved by the fact that when heated above its melting point, or boiled with dilute sulphuric acid, it is converted with loss of carbon dioxide into *dimethylketodicyclopentanecarboxylic acid* melting at 180° (p. 780).

In this respect, it differs in a marked manner from the B-modification, which remains unaltered even after prolonged boiling with dilute sulphuric acid.

On evaporating the hydrochloric acid mother liquors of the A-acid, a considerable quantity of the B-modification (p. 778) is readily obtained, the proportion of each produced in the experiment described being about 1 of A to 3 of B. The proportion in which these acids are formed, however, depends entirely upon the length of time the mixture is

heated during the process of hydrolysis; should the heating be continued longer than 2 hours, then the A-modification is rapidly decomposed, with formation of the monocarboxylic acid melting at 180° (see next section).

*Action of Dilute Sulphuric Acid on the Yellow Sodium Compound. Formation of Dimethylketodi*cyclo*pentanecarboxylic Acid,*

$$Me_2C<\begin{matrix}C(CO_2H)\cdot CH_2\\ |\quad\quad |\\ CH\text{——}CO\end{matrix}.$$

In carrying out this decomposition, 10 grams of the yellow sodium compound were boiled for 6 hours with a 25 per cent. solution of sulphuric acid, when, on allowing the product to cool, a large quantity of a crystalline acid separated. This was collected, recrystallised from water, and analysed:

0·1960 gave 0·4481 CO_2 and 0·1163 H_2O. C = 62·3; H = 6·6.
$C_8H_{10}O_3$ requires C = 62·3; H = 6·6 per cent.

*Dimethylketodi*cyclo*pentanecarboxylic acid* separates from water, in which it is sparingly soluble, in fern-like needles, and melts at 180°; when carefully heated, it sublimes in long, silky needles. It is moderately soluble in hot benzene, and crystallises out on cooling in small plates. The aqueous solution of the acid gives no coloration with ferric chloride; but if the crystals of the acid are moistened with fuming nitric acid, a deep red solution is produced.

The *silver* salt, $C_8H_9O_3Ag$, separates from a neutral solution of the ammonium salt on the addition of silver nitrate, as a white, crystalline precipitate, which dissolves in much boiling water, and crystallises out, on cooling, in long needles.

0·1101 gave 0·1492 CO_2, 0·0369 H_2O, and 0·0450 Ag.
= 36·9; H = 3·7; Ag = 41·0.
$C_8H_9O_3Ag$ requires C = 36·8; H = 3·5; Ag = 41·3 per cent.

The *semicarbazone*, $C_7H_{10}O_2\cdot C{:}N_2H\cdot CO\cdot NH_2$, separates as an insoluble, sandy precipitate when a mixture of the acid, sodium acetate, and semicarbazide hydrochloride, dissolved in water, is boiled for a few minutes. It crystallises from dilute acetic acid in long, silky needles, which decompose at 255°.

0·1412 gave 25 c.c. nitrogen at 15° and 750 mm. N = 20·4.
$C_9H_{13}O_3N_3$ requires N = 20·0 per cent.

The *hydrazone*, $C_7H_{10}O_2\cdot C{:}N_2H\cdot C_6H_5$, is formed when a solution of phenylhydrazine in glacial acetic acid is added to an aqueous solution of the acid and the mixture boiled for a short time. It separates from dilute acetic acid in yellow needles, which decompose at 217°.

0·1849 gave 19 c.c. nitrogen at 16° and 767 mm. N = 12·2.
$C_{14}H_{16}O_2N_2$ requires N = 11·4 per cent.

This hydrazone is very sparingly soluble in water, but dissolves readily in sodium carbonate solution.

The yield of dimethylketodi*cyclo*pentanecarboxylic acid, obtained from the yellow sodium compound in the way described above, is about 30 per cent. of the theoretical, and the aqueous liquors from which it has crystallised give, on extraction with ether and evaporating, a crystalline residue, which consists entirely of the B-modification of dimethylketodi*cyclo*pentanedicarboxylic acid (p. 778). In preparing the monocarboxylic acid, it was found most convenient to extract the product of hydrolysis of the yellow sodium compound (see above) with ether, and after evaporating off the ether, to heat the residue with water in sealed tubes at 180° for 5 hours, when the B-modification of the dibasic acid is also completely converted into the monobasic acid. It is evident, therefore, that only the A-modification of the dibasic acid is converted into the monobasic acid during the hydrolysis of the yellow sodium compound with sulphuric acid, the B-modification remaining unchanged. It has previously been mentioned (p. 779) that the B-modification is stable to dilute sulphuric acid.

*Oxidation of Dimethylketodi*cyclo*pentanecarboxylic Acid. Formation of αα-Dihydroxy-ββ-dimethylglutaric Acid,* $CO_2H{\cdot}C(OH)_2{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2H$, *and of αα-Dimethylsuccinic Acid,* $CO_2H{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2H$.

The solution of the ketonic acid in sodium carbonate is only very slowly oxidised by potassium permanganate at the ordinary temperature, and it was found necessary, in order to facilitate oxidation, to heat the mixture at about 80—90°. About 12 grams of the acid dissolved in sodium carbonate were mixed with a small quantity of permanganate and heated on the water-bath for twelve hours, further quantities of permanganate being added from time to time as soon as the pink colour became discharged. The excess was then removed by sulphur dioxide, and the solution, after filtering, evaporated to a small bulk, acidified, and extracted with ether. The solid residue obtained on evaporating the ethereal solution was then recrystallised from chloroform, from which it separated in prismatic, apparently homogeneous, needles melting between 84° and 90°.

0·1774 gave 0·3026 CO_2 and 0·0982 H_2O. C = 46·5 ; H = 6·1.
$C_7H_{12}O_6$ requires C = 43·8 ; H = 6·2 per cent.

For a long time we were unable to discover the nature of this substance, but ultimately it was shown to consist of a mixture of αα-di-

hydroxydimethylglutaric acid and *aa*-dimethylsuccinic acid. These acids are exceedingly difficult to separate by crystallisation, but the separation was eventually effected by taking advantage of the difference in the properties of their calcium salts. The mixed acids were dissolved in water, excess of ammonia and calcium chloride was added, and the mixture allowed to stand, when a crystalline, very sparingly soluble salt gradually began to separate, the separation being complete in 12 hours.

The calcium salt was collected, washed, dried at 100°, and by analysis and isolation of the acid proved to be the calcium salt of *aa*-dihydroxydimethylglutaric acid.

0·3150 gave 0·1858 $CaSO_4$. Ca = 17·1.

$C_7H_{10}O_6Ca$ requires Ca = 17·3 per cent.

To obtain the acid, the calcium salt was suspended in cold water and acidified with excess of hydrochloric acid, ammonium sulphate was then added, and the solution repeatedly extracted with ether. The solid extract separated from chloroform in needles melting at 84°, and proved to be *aa-dihydroxydimethylglutaric acid* (see p. 757).

0·1706 gave 0·2761 CO_2 and 0·1006 H_2O. C = 44·1; H = 6·5.
0·1448 „ 0·2322 CO_2 „ 0·0851 H_2O. C = 43·7; H = 6·5.

$C_7H_{12}O_6$ requires C = 43·8; H = 6·2 per cent.

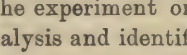
The filtrate from the calcium salt of this acid, on boiling, deposited a further small quantity of a calcium salt. This was collected, decomposed with hydrochloric acid, and extracted with ether. The solid residue which was obtained on evaporating off the ether crystallised from water, in which it was exceedingly soluble, in small prisms melting at 137—138°.

0·1791 gave 0·3233 CO_2 and 0·1101 H_2O. C = 49·2; H = 6·8.

$C_6H_{10}O_4$ requires C = 49·3; H = 6·8 per cent.

A careful examination of this acid proved it to be *aa-dimethylsuccinic acid.* By far the larger proportion of the acids produced in this oxidation consists of *aa*-dihydroxydimethylsuccinic acid, since from the 12 grams used in the experiment only enough dimethylsuccinic acid was obtained for analysis and identification.

*Reduction of Dimethylketodic*cyclo*pentanecarboxylic Acid. Formation of Dimethylketopentamethylenecarboxylic Acid,*



This acid is obtained when a solution of dimethylketodi*cyclo*pentanecarboxylic acid (7 grams) in dilute sodium carbonate is allowed

to remain in contact with 3 per cent. sodium amalgam (300 grams) in a flat porcelain dish for 12 hours with frequent stirring, a current of carbon dioxide being led through the liquid during the whole operation.

The solution, after filtering and acidifying, was saturated with ammonium sulphate and extracted several times with ether. The ethereal solution was then evaporated, when a solid acid was obtained which crystallised from water in small prisms.

0·1729 gave 0·3898 CO_2 and 0·1221 H_2O. C = 61·5; H = 7·8.
$C_8H_{12}O_3$ requires C = 61·5; H = 7·7 per cent.

Dimethylketopentamethylenecarboxylic acid melts at 103°, and is readily soluble in water. When heated in small quantities, it distils unchanged.

The *oxime*, $C_7H_{12}O_2C{:}N{\cdot}OH$, was prepared by dissolving the acid in dilute sodium carbonate and adding an excess of hydroxylamine hydrochloride. After standing for 2 days, the solution was acidified, saturated with ammonium sulphate, and extracted at least 20 times with ether, since the substance is only extracted with difficulty from its aqueous solution by this solvent. The ethereal solution, after drying over calcium chloride and evaporating to a small bulk, deposited the oxime in the form of crystalline crusts, which are very sparingly soluble in ether, and melt at 188—190° with decomposition.

0·1708 gave 12·6 c.c. nitrogen at 17° and 746 mm. N = 8·4.
$C_8H_{13}O_3N$ requires N = 8·2 per cent.

The *semicarbazone*, $C_7H_{12}O_2C{:}N_2H{\cdot}CO{\cdot}NH_2$, separates on boiling the acid with a solution of semicarbazide hydrochloride and sodium acetate as a white, sandy precipitate which crystallises from a large volume of hot water in small needles and decomposes at 215°.

0·2077 gave 35·2 c.c. nitrogen at 19·5° and 760 mm. N = 19·4.
$C_9H_{15}O_3N_3$ requires N = 19·7 per cent.

Dimethylhydroxypentamethylenecarboxylic acid,

$$Me_2C\begin{<}CH(CO_2H){\cdot}CH_2\\ CH_2\text{———}CH{\cdot}OH\end{<}.$$

This acid is formed when dimethylketodi*cyclo*pentanecarboxylic acid is treated with a large excess of sodium amalgam, and is obviously produced by the reduction of the ketonic acid described in the last section.

In preparing it, 7 grams of dimethylketodi*cyclo*pentanecarboxylic acid, dissolved in sodium carbonate, are left in contact with at least 600 grams of 3 per cent. sodium amalgam for 24 hours; the product

is then acidified, extracted repeatedly with ether, and the ethereal extract, after drying over calcium chloride, evaporated.

The crystalline residue dissolves readily in hot water, and on cooling, a small quantity of dimethylketopentamethylenecarboxylic acid separates first. This is removed by filtration, the filtrate rendered alkaline with ammonia, excess of calcium chloride added, and the solution boiled, when a large quantity of a sparingly soluble calcium salt is gradually deposited.

The salt is collected, washed with water, decomposed with hydrochloric acid, and the solution, after saturating with ammonium sulphate, extracted repeatedly with ether. On evaporating off the ether and crystallising the residue from benzene, the pure hydroxy-acid is obtained in the form of small needles.

0·1845 gave 0·3898 CO_2 and 0·1488 H_2O. C = 60·6 ; H = 8·9.
$C_8H_{14}O_3$ requires C = 60·8 ; H = 8·8 per cent.

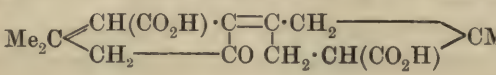
Dimethylhydroxypentamethylenecarboxylic acid melts at 115° and is very soluble in water. It dissolves readily in hot benzene, but is rather sparingly soluble in this solvent in the cold.

Action of Sulphuric Acid.—When the hydroxy-acid is mixed with a large excess of sulphuric acid, a slight rise of temperature takes place, and, at the same time, large quantities of sulphur dioxide are evolved. The evolution of gas ceases after 3 hours if the mixture is left at the ordinary temperature, and on pouring the product into cold water, a curious green solid separates. When thoroughly washed with boiling water and dried, this substance is an olive-green, amorphous powder which gradually becomes yellow on exposure to the air. This green substance is evidently of very high molecular weight, since it melts above 300° ; it dissolves in sodium carbonate, forming a reddish-brown solution, from which the original green compound is precipitated on acidifying. It dissolves in glacial acetic acid, forming an intense indigo-blue solution, the colour of which, on standing, gradually changes to a dark brown.

The filtrate from the calcium salt of the hydroxy-acid (see above) was acidified, evaporated to dryness, and extracted with ether, when a substance was obtained which separated from dilute acetone as a microcrystalline powder. On analysis :

0·1865 gave 0·4438 CO_2 and 0·1272 H_2O. C = 65·1 ; H = 7·6.
$C_{16}H_{22}O_5$ requires C = 65·3 ; H = 7·5 per cent.

This substance, which melts at 205° with partial sublimation, most probably has the constitution represented by the formula,



that is to say, it is produced by the condensation of 2 mols. of dimethylketopentamethylenecarboxylic acid by the alkali formed during the reduction. It has been found that this substance is only produced if the reduction described above is conducted without neutralising the caustic soda formed; if a rapid stream of carbon dioxide is passed during the reduction, no trace of the substance melting at 205° appears to be formed.

Oxidation of Dimethylketopentamethylenecarboxylic Acid. Formation of αα-Dimethylsuccinic Acid, $CO_2H{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2H$, *and ββ-Dimethylglutaric Acid,* $CO_2H{\cdot}CH_2{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2H$.

I. *Oxidation with strong Nitric Acid.*—The ketonic acid (3 grams) was dissolved in strong nitric acid, and heated on the water-bath until the evolution of red fumes had ceased. On evaporating repeatedly to dryness with water, a solid residue was obtained which separated from dilute hydrochloric acid in small prisms and melted at 137—138°.

0·2150 gave 0·3887 CO_2 and 0·1298 H_2O. C = 49·3; H = 6·7.
$C_6H_{10}O_4$ requires C = 49·3; H = 6·8 per cent.

That this acid was *αα-dimethylsuccinic acid* was shown by dissolving it in excess of ammonia, adding calcium chloride, and boiling, when the characteristic calcium salt separated at once.

The remainder of the acid was digested with acetyl chloride and evaporated, when the anhydride of dimethylsuccinic acid was obtained in crystals melting at 29°.

II. *Oxidation with dilute Nitric Acid.*—The ketonic acid (3 grams) was heated with dilute nitric acid (sp. gr. 1·2) on the water-bath until the evolution of red fumes had ceased. The solution was then evaporated to dryness and the solid residue recrystallised three times from dilute hydrochloric acid. The crystals thus obtained were further recrystallised from ether and then analysed:

0·3141 gave 0·6025 CO_2 and 0·2092 H_2O. C = 52·3; H = 7·4.
$C_7H_{12}O_4$ requires C = 52·5; H = 7·5 per cent.

This acid melted at 101—102°, and on treatment with acetic anhydride yielded an anhydride melting at 123°; it therefore consisted of *ββ-dimethylglutaric acid,* $CO_2H{\cdot}CH_2{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2H$ (Perkin and Goodwin, Trans., 1896, **69**, 1474).

Action of Methyl Iodide on the Yellow Sodium Compound. Formation of Ethyl Trimethylketodicyclopentanetricarboxylate,

$$Me_2C<\begin{matrix}C(CO_2Et)\cdot CMe\cdot CO_2Et\\ C(CO_2Et)\cdot CO\end{matrix}.$$

In order to prepare this compound, 25 grams of the pure yellow sodium compound were dissolved in 75 grams of boiling ethyl alcohol, three times the theoretical quantity of methyl iodide (26 grams) were added, and the mixture was heated on the water-bath for 24 hours, at the end of which time it was found that the original deep yellow colour of the solution had entirely disappeared. After distilling off the alcohol and unchanged methyl iodide, the oil which separated on the addition of water was extracted with ether, and the ethereal solution shaken repeatedly with dilute sodium carbonate to remove some substance which dissolves with a yellow colour.

The ethereal solution was then dried over calcium chloride, the ether distilled off, and the residual oil fractionated under 20 mm. pressure, when almost the whole quantity distilled at 219° as a colourless oil.

I. 0·1873 gave 0·4101 CO_2 and 0·1205 H_2O. C = 59·7; H = 7·1.
II. 0·1979 „ 0·4347 CO_2 „ 0·1273 H_2O. C = 59·9; H = 7·1.
$C_{17}H_{24}O_7$ requires C = 60·0; H = 7·0 per cent.

This ester, which is produced almost quantitatively by the process described above, is sharply distinguished from the unmethylated ester (p. 763) by the fact that its alcoholic solution gives no coloration with ferric chloride.

Action of Methyl Alcoholic Potash on Ethyl Trimethylketodicyclopentanetricarboxylate. Formation of the Potassium Salt,

$$Me_2C<\begin{matrix}C(CO_2K)\cdot CMe\cdot CO_2K\\ C(CO_2K)\cdot CO\end{matrix},$$

and Trimethylketodicyclopentanedicarboxylic Acid,

$$Me_2C<\begin{matrix}C(CO_2H)\cdot CMe\cdot CO_2H\\ CH\text{———}CO\end{matrix}.$$

—The pure ethyl ester (20 grams) was mixed with a filtered solution of 20 grams of caustic potash in methyl alcohol and allowed to stand in the cold, when a heavy, crystalline precipitate of a potassium salt gradually formed, the separation being complete in 2 hours. The precipitate was collected, washed with methyl alcohol, dried at 100°, and analysed:

0·3121 gave 0·2186 K_2SO_4. K = 31·4.
$C_{11}H_9O_7K_3$ requires K = 31·6 per cent.

This salt, which evidently has the formula represented at the head of this section, is readily soluble in water, but all attempts to obtain the free tribasic acid were unsuccessful, since the solution of the potassium salt on acidifying is decomposed with evolution of carbon dioxide and formation of *trimethylketodi*cyclo*pentanedicarboxylic acid.* This acid is obtained, by extracting the solution repeatedly with ether, and distilling off the ether, as a colourless solid, which is very soluble in water and crystallises from benzene in lustrous plates melting indefinitely at 70—80°.

These crystals apparently contain water or benzene of crystallisation; on heating, they become yellow and the melting point gradually rises to 146°, when it remains constant, and the substance becomes colourless again.

0·1859 gave 0·3848 CO_2 and 0·0941 H_2O. C = 56·4; H = 5·6.
$C_{10}H_{12}O_5$ requires C = 56·6; H = 5·6 per cent.

The *silver* salt, $C_{10}H_{10}O_5Ag_2$, was obtained on adding silver nitrate to a neutral solution of the ammonium salt as a white precipitate, which on analysis furnished the following results:

0·3214 gave 0·1620 Ag. Ag = 50·41.
$C_{10}H_{10}O_5Ag_2$ requires Ag = 50·57 per cent.

*Trimethylketodi*cyclo*pentanecarboxylic Acid*, $Me_2C<\begin{matrix}C(CO_2H)\cdot CHMe\\ |\\ CH\text{——}CO\end{matrix}$.

When the dibasic acid, described in the last section, is dissolved in a little water and heated in a sealed tube at 180° for 6 hours, it is completely decomposed with elimination of carbon dioxide and formation of the corresponding monobasic acid, the formula of which is given above. This acid separates from water, in which it is only sparingly soluble in the cold, in lustrous plates which melt at 134°.

0·14 gave 0·3297 CO_2 and 0·0898 H_2O. C = 64·2; H = 7·1.
$C_9H_{12}O_3$ requires C = 64·3; H = 7·1 per cent.

The *semicarbazone*, $C_8H_{12}O_2\cdot C{:}N\cdot NH\cdot CO\cdot NH_2$, is precipitated as a sandy powder when an aqueous solution of the acid is boiled with semicarbazide hydrochloride and sodium acetate; it melts with decomposition at about 230°.

0·1408 gave 23·7 c.c. nitrogen at 16° and 746 mm. N = 19·2.
$C_{10}H_{15}O_3N_3$ requires N = 18·7 per cent.

*Action of Alcoholic Potash on Ethyl Trimethylketodi*cyclo*pentanetricarboxylate. Formation of the Lactone of* trans-*Trimethylhydroxybutanetricarboxylic Acid*, $Me_2C<\begin{matrix}C(CO_2H)\\CH_2\cdot CO\cdot O\end{matrix}>\begin{matrix}CHMe\\CO_2H\end{matrix}$.

It has been mentioned in the introduction (p. 744) that the action of boiling ethyl alcoholic potash on ethyl trimethylketodi*cyclo*pentanetricarboxylate proceeds in quite a different way from that of cold methyl alcoholic potash; in the latter case, the di*cyclo*pentane remains intact, whereas in the former it suffers disruption at two points, yielding the lactone represented above.

The pure ester (50 grams) was mixed with an equal weight of potash dissolved in ethyl alcohol and the solution boiled for 12 hours, when the action was complete. The product was evaporated to dryness to remove alcohol, dissolved in a little water saturated with ammonium sulphate and extracted repeatedly with ether, but, after drying over calcium chloride and distilling off the ether, only a small quantity of a thick gum was obtained. As ether was evidently unable to extract the acid from its aqueous solution, the whole was mixed with sand, evaporated to dryness, and extracted in a Soxhlet apparatus with dry ether. It was then noticed that the ether gradually extracted a white substance which was very sparingly soluble and separated out in the flask, but even after the process had been continued for 4 days the extraction of this white substance was far from complete. When, however, acetone was substituted for ether, very satisfactory results were obtained.

The method we ultimately adopted in extracting this acid from the acidified product of the hydrolysis was to evaporate to dryness and thoroughly extract the dried product in the Soxhlet apparatus with ether, in order to remove a trace of oily impurity soluble in ether and then to extract with pure acetone. On evaporating off the acetone, a large quantity of a solid remained which, after washing with ether melted at 225—227° with evolution of aqueous vapour. When boiled with water, this substance gradually dissolved, and on cooling slowly, large, colourless prisms were deposited which melted at 237° with decomposition.

0·1908 gave 0·3588 CO_2 and 0·1047 H_2O. C = 51·3; H = 6·1.
$C_{10}H_{14}O_6$ requires C = 52·1; H = 6·1 per cent.

This *lactone* of *trimethylhydroxybutanetricarboxylic acid* is a remarkably stable substance; it does not appear to be acted on by dry hydrobromic acid in the cold, and its solution in sodium carbonate may be

boiled with permanganate for a considerable time without appreciable oxidation taking place. It is unchanged by boiling dilute sulphuric acid, and is not altered by heating with water in a sealed tube at 180°. It is very sparingly soluble in the usual organic solvents, excepting acetone, and dissolves moderately in hot water but only sparingly in the cold.

The *silver* salt, $C_{10}H_{12}O_6Ag_2$, separates from a neutral solution of the ammonium salt, on the addition of silver nitrate, as a white, crystalline precipitate, which dissolves appreciably in hot water and crystallises out on cooling in plates.

0·1967 gave 0·1929 CO_2, 0·0492 H_2O, and 0·0952 Ag.
C = 26·9 ; H = 2·8 ; Ag = 48·4.
$C_{10}H_{12}O_6Ag_2$ requires C = 27·0 ; H = 2·7 ; Ag = 48·6 per cent.

The *barium* salt of the hydroxytricarboxylic acid, $(C_{10}H_{13}O_7)_2Ba_3$, was prepared by dissolving the lactone acid in water, heating to boiling in a Jena flask, and adding clear hot barium hydroxide solution in small quantities at a time, so that the solution was kept always slightly alkaline. A sparingly soluble barium salt gradually separated in the form of a sandy powder, and after boiling for 2 hours (air being carefully excluded from the flask) the salt was collected on the pump, rapidly washed with hot water, and dried at 100°.

0·3910 gave 0·3048 $BaSO_4$. Ba = 45·8.
$C_{20}H_{26}O_{14}Ba_3$ requires Ba = 45·6 per cent.

The *anhydride*, $\begin{matrix}CH_2\cdot CMe_2\\ |\\ CO\text{——}O\end{matrix}\!>\!C\!<\!\begin{matrix}CO\text{——}O\\ |\\ CHMe\cdot CO\end{matrix}$, may be prepared by boiling the lactonic acid with acetyl chloride for 4 hours. The acid gradually dissolves, and hydrogen chloride is evolved, but the process proceeds very slowly and generally some of the unchanged acid separates on cooling, so that it is necessary to filter the solution and boil the residue again with acetyl chloride. On allowing the solution to evaporate over potash in an exhausted desiccator, large crystals gradually separate: these are collected, ground to a fine powder, and left over potash until the odour of acetic anhydride has entirely disappeared. The substance then melts indefinitely and when treated with benzene a small quantity of a crystalline compound remains undissolved; if this is removed by filtration and the solution concentrated and allowed to stand out of contact with the air, the pure anhydride crystallises out. On analysis:

0·1896 gave 0·3924 CO_2 and 0·1005 H_2O. C = 56·5 ; H = 5·9.
$C_{10}H_{12}O_5$ requires C = 56·6 ; H = 5·6 per cent.

This substance melts at 94—96° and is insoluble in cold sodium

carbonate solution; that it is the anhydride of the *trans*-acid is shown by the fact that when boiled with water it is slowly converted into this acid.

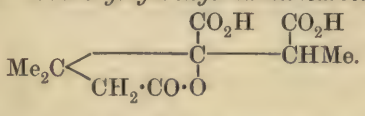
Action of Phosphorus Pentachloride on the trans-*Lactone. Formation of Ethyl Trimethylchlorobutanetricarboxylate*, $CO_2Et\cdot CH_2\cdot CMe_2\cdot CCl(CO_2Et)\cdot CHMe\cdot CO_2Et$. —On heating 2 grams of the lactonic acid with 6 grams of phosphorus pentachloride on the water-bath, it gradually dissolved, and after 2 hours no unchanged substance separated on cooling. The whole was poured into well cooled alcohol and, after standing for some time, water was added, and the oil extracted with ether. The ethereal solution was shaken with sodium carbonate, dried over calcium chloride, and the residual oil allowed to remain over sulphuric acid in a desiccator until free from ether.

0·2494 gave 0·1 AgCl. Cl = 9·9.

$C_{16}H_{27}O_6Cl$ requires Cl = 10·1 per cent.

This substance could not be purified by distillation as it decomposes even under greatly reduced pressures.

Lactone of cis-*Trimethylhydroxybutanetricarboxylic Acid*,

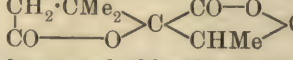


When the *trans*-acid (m. p. 237°) is distilled under 30 mm. pressure, an oil passes over at 267°, which solidifies, on cooling, to a crystalline mass. As the distillate was found to be partly soluble and partly insoluble in dilute sodium carbonate, and therefore evidently consisted of a mixture of acid and anhydride, it was boiled with water, and the solution concentrated and cooled, when microscopic needles separated, which melted at 181° and decomposed with evolution of aqueous vapour at 200°.

0·1834 gave 0·3499 CO_2 and 0·1030 H_2O. C = 52·0; H = 6·2.

$C_{10}H_{14}O_6$ requires C = 52·1; H = 6·1.

This *cis*-acid is much more soluble in water than the *trans*-acid, but like the latter it is a very stable substance, and is only very slowly attacked by boiling alkaline permanganate.

The Anhydride,  . —The *cis*-acid is instantly attacked by acetyl chloride on warming, with evolution of hydrogen chloride, and on evaporating over potash a solid residue is obtained which is quite insoluble in cold sodium carbonate solu-

tion. This anhydride crystallises from benzene in lustrous plates, melts at 131°, and when boiled with water is reconverted into the *cis*-acid.

0·1816 gave 0·3751 CO_2 and 0·0942 H_2O. C = 56·3; H = 5·7.
$C_{10}H_{12}O_5$ requires C = 56·6; H = 5·6 per cent.

When the *cis*-lactonic acid is treated with phosphorus pentachloride and the product poured into alcohol, exactly as in the case of the *trans*-acid, an oil is obtained which decomposes when distilled.

0·2501 gave 0·101 AgCl. Cl = 10·0.
$C_{16}H_{27}O_6Cl$ requires Cl = 10·1 per cent.

This oil is evidently *ethyl trimethylchlorobutanetricarboxylate*, but there is no evidence to show whether this is identical or not with the substance of the same composition obtained from the *trans*-acid.

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BRAZILIN AND HÆMATOXYLIN. PART I.

BY

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W. H. PERKIN, JUN.,

AND

J. YATES.

From the Transactions of the Chemical Society, 1901. Vol. 79.

CXLVI.—*Brazilin and Hæmatoxylin. Part I.*

By A. W. Gilbody, W. H. Perkin, jun., and J. Yates.

Brazil-wood, or Red-wood, which was originally imported from the East Indies, has been used in Europe for dyeing purposes from very early times and certainly before the discovery of America.

Thus, about the year 1190, the Spanish writer Kimichi mentions dye-woods called Bresil or Brasil (from *braza*, fiery-red), and when the Spaniards discovered South America in 1500, it is probable that they named the northerly portion Brazil, after the dye-wood which is found there in such immense quantities. The Brazil-wood tree belongs to the *Leguminosæ*, species *Cæsalpinia*, and is widely distributed in the Tropics, in the East Indies, South and Central America, the Antilles, and Africa. The most valued Brazil-wood (Fernambukholz, bois de Fernambouc) is obtained from *Cæsalpinia Crista* and *C. brasiliensis*, large crooked trees, with knotty stems, which occur in great numbers in the forests of Brazil and Jamaica.

The wood, which comes into the market in round blocks, is very hard and of a deep red colour; when freshly cut, the colour is light yellow, but this rapidly changes to red in contact with the air. The crude material is rasped and extracted, either by simply boiling with water, or by heating with water under pressure, the liquid is then concentrated in vacuum pans, the actual extract sent into the market varying very much in strength.

Brazil-wood extract is still used in dyeing, but to a comparatively limited extent, owing to the fugitive character of the colours which it yields. It is fixed on the fibre usually in the form of its aluminium or tin lakes, which, although less brilliant and fast than the corresponding alizarine lakes, are somewhat similar to these in appearance.

Brazilin, the actual colouring matter of Brazil-wood, often separates from the commercial extracts in the form of dark brown, crystalline crusts, and pure brazilin is comparatively easily obtained from this crude material by repeated recrystallisation from water containing a small quantity of sulphurous acid, from which solution it separates in pale yellow prisms. The first chemist to isolate brazilin in a crystal-

line form appears to have been Chevreul (*Ann. Chim.*, 1808, [i], **66**, 225), but no attempt was made to determine its constitution until Bolley (*Schweiz. polyt. Zeitsch.*, 1864, **9**, 267) suggested the formula $C_{22}H_{20}O_7$, as the result of several analyses; Kopp (*Ber.*, 1873, **6**, 446) subsequently repeated the analyses and considered the formula $C_{22}H_{18}O_7$ as more probable. It was, however, left to Liebermann and Burg (*Ber.*, 1876, **9**, 1883) to determine accurately the composition of brazilin, and the formula, $C_{16}H_{14}O_5$, which they proposed is that which is used at the present day. The first important step which afforded any evidence of the constitution of brazilin is due to Kopp (*loc. cit.*), who showed that when submitted to dry distillation, this substance yields, besides tar, considerable quantities of resorcinol and, indeed, the yield is so good that this method was for a long time used for its preparation. Before this, Bolley (*loc. cit.*) had treated brazilin with nitric acid and obtained a yellow substance which he imagined to be picric acid, but which Reim (*Ber.*, 1871, **4**, 334) subsequently showed was trinitroresorcinol or styphnic acid, $C_6H(NO_2)_3(OH)_2$.

At a somewhat later date, Liebermann and Burg (*loc. cit.*) showed that resorcinol is also produced in quantity when brazilin is fused with potash, and thus it was early recognised that brazilin is a derivative of resorcinol. The same chemists also proved that brazilin contains four hydroxy-groups, since when treated with acetic anhydride it is converted into a crystalline, colourless, *tetracetyl* derivative, $C_{16}H_{10}O(OAc)_4$. This was subsequently confirmed by Dralle (*Ber.*, 1884, **17**, 375) who, by treating brazilin with sodium methoxide and methyl iodide, obtained *trimethylbrazilin*, $C_{16}H_{10}O(OMe)_3{\cdot}OH$, a substance which still contains a hydroxyl group, since it yields an acetyl compound and when heated in benzene solution with sodium and methyl iodide at 120° is converted into *tetramethylbrazilin*, $C_{16}H_{10}O(OMe)_4$. Of the four hydroxy-groups in brazilin, three are therefore easily methylated, whereas the fourth is not; for this reason it was assumed that whereas the three are aromatic or phenolic, the fourth is alcoholic, and a further examination of the properties of brazilin has shown that this assumption is correct.

When brazilin is oxidised, it loses two atoms of hydrogen and is converted into *brazilein*,

$$C_{16}H_{14}O_5 + O = C_{16}H_{12}O_5 + H_2O.$$

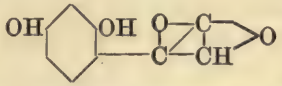
This change takes place under various conditions; thus Liebermann and Burg (*loc. cit.*) obtained crude brazilein by exposing an alkaline solution of brazilin to the air and by treating an alcoholic solution of brazilin with iodine. Hummel and A. G. Perkin (*Ber.*, 1882, **15**, 2343) prepared pure crystalline brazilein by passing air through a solution of brazilin in ammonia. Buckha and Erck (*Ber.*, 1884, **17**,

685; 1885, **18**, 1140) obtained brazilein by oxidising brazilin with small quantities of nitric acid, and Schall and Dralle (*Ber.*, 1890, **23**, 1433) by treating its solution in glacial acetic acid with sodium nitrite.

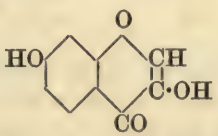
If air is passed through a solution of brazilin in dilute alkali for a considerable time, the purple colour of the solution gradually changes to a reddish-brown and the brazilein which is first produced is completely oxidised. Schall and Dralle (*Ber.*, 1888, **21**, 3017; 1889, **22**, 1559; 1892, **25**, 19), who first studied this oxidation, isolated from the product β-resorcylic acid,

and a substance, $C_9H_6O_4$, which crystallised in needles melting at 271° and contained two hydroxyl groups, since it yielded a *diacetyl* compound, $C_9H_4O_2(OAc)_2$, and a *dimethyl ether*, $C_9H_4O_2(OMe)_2$.

This dimethyl ether, on treatment with acetic acid and permanganate, is oxidised to p-*methoxysalicylic acid*, $C_6H_3(OMe)(OH)\cdot CO_2H$, and on this account and also because the substance $C_9H_6O_4$ does not combine with hydroxylamine or phenylhydrazine, they first assigned to it the constitution

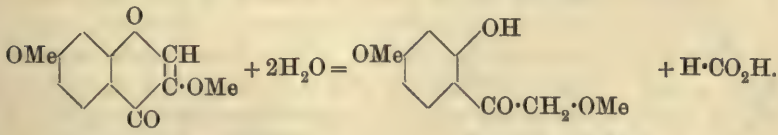


Schall (*Ber.*, 1894, **27**, 528) afterwards suggested that this substance, $C_9H_6O_4$, might possibly be a *phenyl-γ-pyrone* derivative of the formula



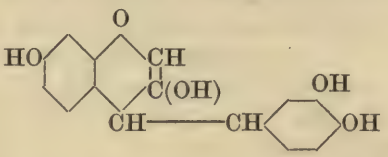
and this view was subsequently proved by Feuerstein and Kostanecki (*Ber.*, 1899, **32**, 1025) to be correct.

These chemists showed that when the dimethyl ether of this substance is boiled with sodium ethoxide it is converted into fisetol dimethyl ether (Herzig, *Monatsh.*, 1891, **12**, 187) with elimination of formic acid, a decomposition which is evidently represented thus:



Dimethyl ether of $C_9H_6O_4$. Fisetol dimethyl ether.

This proof of the constitution of the substance $C_9H_6O_4$, taken in connection with the results which had been obtained by Herzig (*Monatsh.*, 1898, **19**, 738) and by us (see below) led Feuerstein and Kostanecki (*loc. cit.*, p. 1028) to suggest the formula



as probably representing the constitution of brazilin.

Oxidation of Trimethylbrazilin with Potassium Permanganate.

During the course of a long series of experiments on the constitution of brazilin and hæmatoxylin which have been in progress since 1883 and some of the results of which have lately been published as abstracts in the Proceedings (1899, **15**, 27, 75, and 241 ; 1900, **16**, 105 and 107), we have carefully studied the behaviour of trimethylbrazilin, $C_{16}H_{11}O_2(OMe)_3$, with permanganate under very varied conditions. We obtained in this way, besides oxalic, acetic, and formic acids, the following important oxidation products, the investigation of which has thrown much light on the problem of the constitution of brazilin.

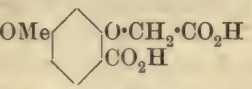
A.	An acid of the formula	$C_{19}H_{18}O_9$,	m. p.	208°.
B.	„	„ $C_{10}H_{10}O_6$,	„	174 .
C.	„	„ $C_{10}H_{10}O_6$,	„	195 .
D.	„	„ $C_{12}H_{12}O_6$,	„	129 .

In the present paper, the description and determination of the constitution of the acids B and C are given in detail, the investigation of the acids A and D, called *brazilinic* and *brazilic* acids respectively, and their decomposition products is not yet complete and will form the subject of a future communication.

Examination of the Acid B of the Formula $C_{10}H_{10}O_6$ *and Melting Point* 174°.—This acid crystallises from water in long needles ; it is dibasic, since it yields a *silver* salt, $C_{10}H_8O_6Ag_2$, it contains one methoxy-group, and when fused with potash is decomposed with formation of a substance which, since it gives with ferric chloride an intense violet coloration, is probably a derivative of resorcinol.

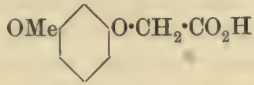
When the aqueous solution of this acid is heated with water at 200°, carbon dioxide is eliminated and a monobasic acid, $C_9H_{10}O_4$ (m. p. 118°), is produced, and this behaviour, taken in conjunction with the fact that brazilin under various conditions yields *p*-methoxy-

salicylic acid, suggested to us that the constitutions of the two acids, $C_{10}H_{10}O_6$ and $C_9H_{10}O_4$, are very probably represented by the formulæ,



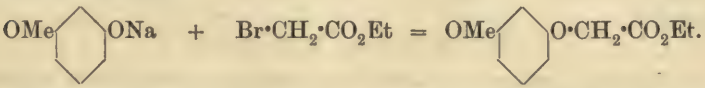
2-Carboxy-5-methoxyphenoxy-acetic acid.

and



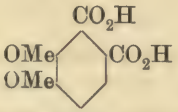
m-Methoxyphenoxy-acetic acid.

In order to prove these formulæ, we determined to attempt the synthesis of the acid $C_9H_{10}O_4$ and ultimately succeeded in doing this by treating the sodium compound of resorcinol monomethyl ether with ethyl bromoacetate.

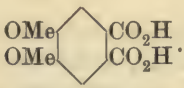


The m-*methoxyphenoxyacetic acid*, which was obtained by hydrolysing the product, melted at 118° and was identical with the acid $C_9H_{10}O_4$ produced by heating the acid $C_{10}H_{10}O_6$. There can therefore be no doubt that the latter is 2-*carboxy*-5-*methoxyphenoxyacetic acid* and has the constitution represented by the formula given above.

Examination of the Acid C of the Formula $C_{10}H_{10}O_6$ *and of Melting Point about* 195°.—This acid crystallised from its dilute aqueous solution in flat prisms containing 2 mols. of water of crystallisation and from concentrated solutions it separated in long, thin needles which were anhydrous. It is a dibasic acid, yielding a *silver* salt, $C_{10}H_8O_6Ag_2$, and an *anhydride* melting at 175°. When heated with hydrochloric acid at 180°, it was completely decomposed into carbon dioxide and catechol, and since it contains two methoxy-groups, its constitution must be represented by one of the formulæ



Hemipinic acid.



m-Hemipinic acid.

Since the melting points, or rather the decomposing points, of these two acids depend so much on the rapidity with which the determination is made and the anhydrides melt at approximately the same temperatures, advantage was taken of the wide difference in the melting points of their ethylimides, $(OMe)_2C_6H_2(CO)_2NEt$, in order to distinguish between them. Goldschmiedt (*Monatsh.*, 1888, **9**, 339) first showed that whereas the ethylimide of hemipinic acid melts at 98°, the corresponding derivative of *m*-hemipinic acid does not melt until 230°. Experiment showed that the ethylimide of the acid from tri-

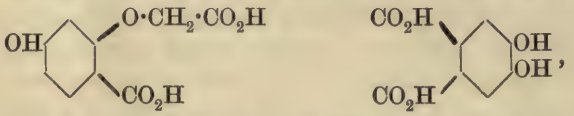
methylbrazilin melted at 230° and therefore there can be no doubt that this acid is m-*hemipinic acid.*

The isolation of *m*-hemipinic acid and of catechol from the products of the oxidation of trimethylbrazilin is a result of great importance, since it proves that brazilin, besides being a resorcinol derivative, also contains a catechol nucleus.

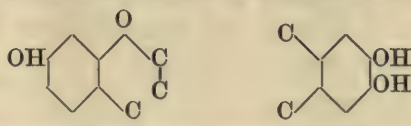
It should be mentioned, however, that shortly before the publication of this result (Proc., 1899, **15**, 27), Herzig (*Monatsh.*, 1898, **19**, 738) had shown that when brazilin is fused with potassium hydroxide it yields a small quantity of an acid which he identified by its melting point and colour reaction with ferric chloride as protocatechuic acid, so that he was actually the first to discover that brazilin is a derivative of catechol.

The Constitution of Brazilin.

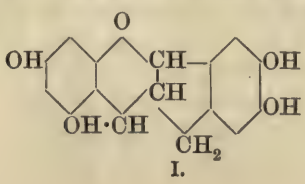
The isolation of 2-carboxy-5-methoxyphenoxyacetic acid and *m*-hemipinic acid from the products of the oxidation of trimethylbrazilin not only proves that brazilin contains both resorcinol and catechol nuclei, but the structure of these acids also affords most valuable evidence as to the way in which these two nuclei are linked together. If the formulæ of the two acids are written side by side without their methyl groups,



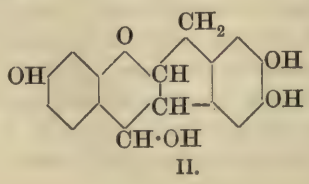
it is clear that in the formula of brazilin these two nuclei must be united in the positions indicated by the dark lines. If now the skeleton formulæ of these two acids be written thus,



it is at once evident that in constructing a constitutional formula for brazilin, $C_{16}H_{14}O_5$, these two residues, which contain C_{17}, must be fused together in such a way that one carbon atom is common to both. Since it is known that in the centre portion, between the two nuclei, brazilin contains an alcoholic hydroxy-group, it seems to us that there can hardly be a doubt that one of the two following formulæ represents the constitution of this substance.

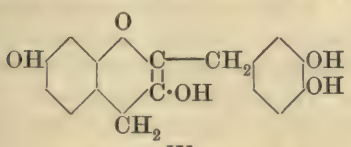


I.

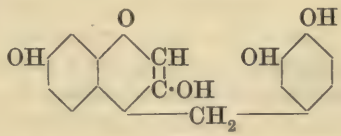


II.

It is obvious that neither formula III, first proposed by Gilbody and Perkin (Proc., 1899, **15**, 75), nor formula IV, suggested by Feuerstein and Kostanecki (*Ber.*, 1899, **32**, 1028),



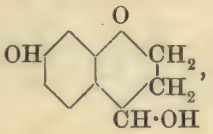
III.



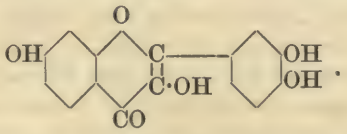
IV.

can possibly represent brazilin, since neither of these gives any explanation of the formation of 2-carboxy-5-methoxyphenoxyacetic acid or of *m*-hemipinic acid by the oxidation of trimethylbrazilin. On the other hand, both formulæ I and II not only account in a satisfactory manner for the formation of these acids, but they are also in agreement with all the other properties of brazilin which are known at the present time.

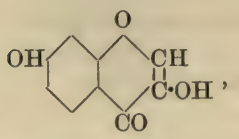
The new formulæ, I and II, represent brazilin as a derivative of a *tetrahydropheno-γ-pyrone* of the formula



a group of atoms that does not appear to have been met with in any of the natural colouring matters hitherto investigated. These formulæ for brazilin are, nevertheless, very similar to those of some of the natural colouring matters and bear considerable resemblance especially to that of fisetin which Herzig (*Monatsh.*, 1894, **15**, 688) and Kostanecki (*Ber.*, 1895, **28**, 2302) have shown to have the constitution

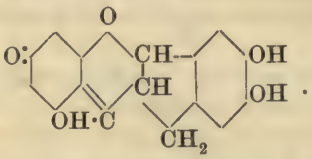


Herzig (*Monatsh.*, 1901, **22**, 209) has lately expressed the opinion that although the formation of 2-carboxy-5-methoxyphenoxyacetic acid and *m*-hemipinic acid from trimethylbrazilin practically proves the position of all the carbon atoms in the molecule, there is still no actual proof of the existence of a γ-pyrone ring in brazilin. Since, however, Feuerstein and Kostanecki (*loc. cit.*) have conclusively proved that the substance $C_9H_6O_4$ obtained by Schall (*loc. cit.*) by passing air through an alkaline brazilin solution is a pheno-γ-pyrone derivative of the formula



it appears to us that there can scarcely be a doubt that brazilin itself also contains a γ-pyrone ring.

As soon as it has been decided which of the formulæ I or II is to be accepted as representing brazilin, $C_{16}H_{14}O_5$, the probable constitution of brazilein, $C_{16}H_{12}O_5$, may be deduced by assuming that the two hydrogen atoms which are removed in the conversion of the former into the latter are derived from the CH·OH group and the hydroxyl group of the resorcinol nucleus. If formula I be taken as an example, the formula of brazilein deduced in this way would be



This relationship between brazilin and brazilein can, however, not be considered proved until it has been found possible to reconvert the latter into the former by reduction.

Preparation of Trimethylbrazilin, $C_{16}H_{11}O_2(OMe)_3$.

The trimethylbrazilin required for this research was prepared by Schall and Dralle's method (*Ber.*, 1888, **21**, 3009), but during the course of the preparation of several kilos. of the substance we found it advantageous to introduce slight modifications into the process, which we now conduct as follows.

Brazilin (143 grams) is dissolved in the smallest possible quantity of hot absolute methyl alcohol, and mixed in a large flask connected with a reflux apparatus, with a solution of sodium (35 grams) in methyl alcohol, an operation which causes the separation of a mass of crystals, consisting probably of the trisodium compound of brazilin. A slight excess of methyl iodide (250 grams) is then added and after well mixing, the flask is immersed in a large water-bath and heated at 60—65° day and night for 50 hours, the temperature being kept constant by a regulator and access of air avoided as far as possible by inserting a stopper of cotton wool into the open end of the condenser. The product is poured into about 6 litres of water, allowed to stand for 24 hours, and the precipitate, after collecting on the pump and washing with water, is transferred to large flasks and extracted with warm ether until all the trimethylbrazilin has been dissolved. The ethereal

extract is shaken repeatedly with sodium hydroxide, dried over calcium chloride and evaporated to a small bulk, when on standing and even during the concentration, the trimethylbrazilin separates as a pale yellow, crystalline mass, which after washing on the pump with ether is almost pure and in this condition was used in all our experiments.

During the extraction of the crude trimethylbrazilin with ether, the impurities first dissolve, the mass becomes more and more sparingly soluble, and ultimately a peculiar, brownish-violet residue is obtained, which closely resembles amorphous phosphorus in appearance and is apparently quite insoluble in ether.

Although somewhat tedious, the purification with ether is much to be preferred, as the alternative method, namely, crystallisation from alcohol, is more wasteful and frequently does not give at once so pure a product. The yields we obtained usually from 1 kilo. of brazilin were 950 grams of crude product, which on extraction with ether yielded about 700 grams of trimethylbrazilin and 60 grams of the brownish-violet, insoluble residue, the remainder consists largely of dimethylbrazilin which is dissolved out during the treatment of the ether extract with sodium hydroxide, and partly of uncrystallisable resins remaining in the ethereal mother liquors of the trimethylbrazilin.

A specimen of trimethylbrazilin which had been purified by recrystallisation from ether was analysed with the following results:

0·1612 gave 0·4102 CO_2 and 0·0888 H_2O. C = 69·4; H = 6·1.
$C_{16}H_{11}O_2(OMe)_3$ requires C = 69·5; H = 6·1 per cent.

A methoxyl determination by Zeisel's method gave the following result:—

0·2121 gave 0·4631 AgI. OCH_3 = 29·1.
$C_{16}H_{11}O_2(OMe)_3$ requires OH_3 = 28·2 per cent.

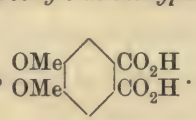
Oxidation of Trimethylbrazilin with Potassium Permanganate.

When ground up into a fine paste with water, trimethylbrazilin is slowly attacked at the ordinary temperature by permanganate and in our earlier experiments much material was oxidised in this way. A long series of comparative trials showed, however, that there was not much difference in the yield of acids produced at 15° and at 90°, and as oxidation is much more rapid at 90°, we have during the last two years worked almost entirely at this temperature. The oxidation is now carried out as follows. Trimethylbrazilin (10 grams) is ground up into an exceedingly fine paste with a little water, washed into a 4-litre flask with about 500 c.c. of hot water, and a cold saturated solution of potassium permanganate added in small quantities at a time, with repeated shaking, the flask being heated during the whole operation on

the water-bath. As soon as the colour of the permanganate remains permanent for several minutes (which is the case after about 1½ hours), the excess is destroyed by the addition of a little sodium sulphite, and the whole filtered on the pump by means of a Buchner funnel.

The manganese precipitate is ground up with hot water and filtered again, and, after repeating this operation, the washings are added to the original filtrate, the whole nearly neutralised with hydrochloric acid and evaporated to a small bulk, first in an enamelled basin over the free flame and then on the water-bath.

During this operation, a small quantity of a crystalline precipitate is usually deposited; this was collected and found to consist of unchanged trimethylbrazilin. On acidifying the cold, slightly brownish-coloured liquid with hydrochloric acid, it becomes pink and deposits a red, resinous precipitate. This is extracted repeatedly with small quantities of chloroform. The chloroform solution is then dried over calcium chloride and evaporated, and the reddish-brown, resinous residue, which contains *brazilinic acid* and *brazilic acid*, treated as described on p. 1410. The aqueous solution, which had been extracted with chloroform, is saturated with ammonium sulphate and extracted at least 20 times with ether. The ethereal solution is then dried over calcium chloride and evaporated to a small bulk, when, on standing, it deposits a yellow, crystalline precipitate, which consists almost entirely of m-*hemipinic* acid and 2-*carboxy*-5-*methoxyphenoxyacetic acid.*

m-*Hemipinic Acid*,  .

The crude mixture of *m*-hemipinic acid and 2-carboxy-5-methoxyphenoxyacetic acid, obtained as just described, was recrystallised once from water with the aid of animal charcoal and then distilled under 55 mm. pressure, when almost the whole quantity passed over at 172° as a yellow oil, which, on cooling, solidified and consisted of a mixture of *m*-hemipinic anhydride and 2-carboxy-5-methoxyphenoxyacetic acid. It was dissolved in the smallest possible quantity of boiling toluene and the crystals which separated on cooling and those obtained by concentrating the toluene filtrate, were finely powdered and extracted repeatedly with small quantities of dilute sodium carbonate. The insoluble m-*hemipinic anhydride* was then crystallised from toluene, from which it separated in pale yellow crystals melting at 175°. On analysis:

0·1661 gave 0·3521 CO_2 and 0·0607 H_2O. C = 57·8; H = 4·0.
$C_{10}H_8O_5$ requires C = 57·7; H = 3·8 per cent.

This anhydride dissolves readily in dilute methyl alcoholic potash,

and if the solution is evaporated until free from the alcohol and then acidified, a woolly mass of needles separates, which, after washing with a little water on the pump, consists of pure m-*hemipinic acid*. On analysis:

0·1168 gave 0·2272 CO_2 and 0·0481 H_2O. C = 53·0; H = 4·5.
$C_{10}H_{10}O_6$ requires C = 53·1; H = 4·4 per cent.

A methoxyl determination by Zeisel's method furnished the following result:

0·3457 gave 0·6890 AgI. OCH_3 = 26·3.
$(OCH_3)_2C_6H_2(CO_2H)_2$ requires OCH_3 = 27·4 per cent.

The pure *m*-hemipinic acid obtained in this way, when moderately rapidly heated, softens at 190° and decomposes quite sharply at 194—195° into water and the anhydride, but other specimens prepared during this research, which had not been purified by conversion into the anhydride, showed a lower and much less sharp melting or decomposing point; according to Goldschmiedt (*Monatsh.*, 1885, **6**, 380), *m*-hemipinic acid melts when rapidly heated at 179—182°, and as there is thus a slight discrepancy in the melting points, it became necessary to sharply characterise the acid from brazilin.

In the first place, it was repeatedly noticed that the latter acid has the property of crystallising in two entirely different ways, thus, when it separates rapidly from a strong solution in hot water, it is obtained in needles which are anhydrous, but if its saturated aqueous solution is allowed to evaporate at the ordinary temperature, glistening prisms are deposited which contain 2 mols. of water of crystallisation, as the following determination shows:

0·4371, at 100°, lost 0·0596 H_2O H_2O = 13·8.
$C_{10}H_{10}O_6,2H_2O$ requires H_2O = 13·7 per cent.

This capability of crystallising in two such distinct forms is one of the characteristics of *m*-hemipinic acid.

m-*Hemipinethylimide*, $(OMe)_2C_6H_2(CO)_2NEt$.—In order to be quite certain that the acid was *m*-hemipinic acid, a small quantity was dissolved in water, made strongly alkaline with ethylamine, evaporated to dryness, and the residue distilled from a small retort. The yellow, crystalline distillate separated from alcohol, in which it is very sparingly soluble, in yellow needles melting at 230° and consisted of pure *m*-hemipinethylimide. On analysis:

0·2241 gave 11·9 c.c. nitrogen at 19° and 757 mm. N = 6·1.
$C_{12}H_{13}O_4N$ requires N = 5·9 per cent.

Goldschmiedt gives 230° as the melting point of the ethylimide of the *m*-hemipinic acid which he obtained from papaverine.

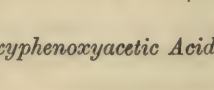
Formation of Catechol from m-*Hemipinic Acid by the Action of Hydrochloric Acid.*—This experiment was carried out before it was known that the acid obtained from trimethylbrazilin was *m*-hemipinic acid. The pure acid (2 grams) was heated in a sealed tube with concentrated hydrochloric acid at 185° for an hour, when on opening the tube there was considerable pressure, and the gas which escaped burnt with a green edged flame and was doubtless methyl chloride. This gas also contained carbon dioxide, as was shown by leading it through baryta water. The contents of the tube were filtered from a few black specks, the filtrate extracted 10 times with ether, and the ether evaporated, when an oily residue was obtained, which on standing over sulphuric acid crystallised in large plates. The crystals were left in contact with a porous tile until quite dry and recrystallised from benzene with the aid of animal charcoal; the colourless prisms thus obtained were analysed:

0·1671 gave 0·4012 CO_2 and 0·0830 H_2O. C = 65·5; H = 5·5.
$C_6H_6O_2$ requires C = 65·5; H = 5·5 per cent.

This substance melted at 104—105° and its solution in water gave with ferric chloride an intense green coloration, which on the addition of ammonium carbonate became first violet and then red. There can be no doubt that it is catechol, since a small quantity mixed intimately with an equal weight of a pure sample of catechol melted at 104°. It is therefore clear that *m*-hemipinic acid, when heated with hydrochloric acid at 185°, is decomposed according to the equation

$$(OMe)_2C_6H_2(CO_2H)_2 + 2HCl = C_6H_4(OH)_2 + 2CO_2 + 2MeCl.$$

This decomposition had not previously been observed, and it is certainly remarkable that the two carboxyl groups attached to the benzene nucleus should be so easily and completely removed at this comparatively low temperature. When hemipinic acid is heated with hydrochloric acid at 170°, it behaves differently, protocatechuic acid being produced by the elimination of only one carboxyl group.

2-Carboxy-5-methoxyphenoxyacetic Acid,  .

The sodium carbonate solution, which had been separated from the *m*-hemipinic anhydride as described on p. 1405, gave, on acidifying, a crystalline precipitate, which was collected and purified by recrystallisation from water, from which it separated in long needles. On analysis:

0·1469 gave 0·2863 CO_2 and 0·0603 H_2O. C = 53·1 ; H = 4·5.
0·1912 ,, 0·3736 CO_2 ,, 0·0777 H_2O. C = 53·1 ; H = 4·4.
$C_{10}H_{10}O_6$ requires C = 53·1 ; H = 4·4 per cent.

2-*Carboxy*-5-*methoxyphenoxyacetic acid* melts at about 174° and seems to have no tendency to form an anhydride, as is shown by the fact that even on distillation it passes over unchanged. It is very sparingly soluble in cold water, but dissolves readily on boiling; it is also sparingly soluble in ether, benzene, or light petroleum, but readily so in methyl alcohol, acetone, or warm acetic acid; from the last of these solvents, it separates on cooling in beautiful, colourless needles. When fused with potassium hydroxide, a product is obtained which, on acidifying and extracting with ether, yields a substance which gives the resorcinol reaction with ferric chloride, and this experiment was the first which afforded us any clue to the constitution of the acid. A determination of the methoxyl group by Zeisel's method was made, with the following result:

0·3784 gave 0·4133 AgI. OCH_3 = 14·40.
$CH_3{\cdot}O{\cdot}C_6H_3(O{\cdot}CH_2{\cdot}CO_2H){\cdot}CO_2H$ requires OCH_3 = 13·72 per cent.

That this acid is dibasic was shown by titration with decinormal sodium hydroxide, when 0·2005 gram of the pure acid required for neutralisation 0·0708 gram NaOH, whereas this amount of an acid, $C_{10}H_{10}O_6$, if dibasic, should neutralise 0·0709 gram NaOH.

The salts of 2-carboxy-5-methoxyphenoxyacetic acid are sufficiently characteristic to be described in some detail.

The *silver* salt, $C_{10}H_8O_6Ag_2$, is obtained as a white, gelatinous precipitate on adding silver nitrate to a slightly alkaline solution of the ammonium salt. On analysis:

0·2565 gave 0·2538 CO_2, 0·0455 H_2O, and 0·1252 Ag. C = 27·0 ; H = 1·9 ; Ag = 48·8.
$C_{10}H_8O_6Ag_2$ requires C = 27·3 ; H = 1·8 ; Ag = 49·1 per cent.

A slightly alkaline solution of the ammonium salt showed the following characteristic behaviour with reagents:

Calcium Chloride gives, in a moderately concentrated solution, a white, amorphous precipitate, which dissolves in warm water, but on boiling separates out again as a very sparingly soluble, amorphous substance. In weaker solutions, calcium chloride gives no precipitate in the cold, but the amorphous calcium salt separates on boiling.

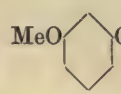
Barium Chloride gives a white, amorphous precipitate which, on warming with water, dissolves, but when the solution is boiled, a very sparingly soluble salt separates in microscopic groups of needles.

Copper Sulphate gives no immediate precipitate in the cold, but, on

standing, an insoluble copper salt slowly separates in pale blue needles; the separation takes place at once on boiling the solution.

Zinc Sulphate.—When this reagent is added to a moderately strong solution of the ammonium salt, the solution remains clear for a few seconds and then suddenly becomes cloudy, owing to the separation of an amorphous zinc salt. If a weak solution is mixed with zinc sulphate and allowed to stand, the zinc salt separates slowly in groups of spherical individuals, which, seen under the microscope, closely resemble yeast cells.

Magnesium Chloride gives no precipitate in the cold, but on boiling, a sparingly soluble salt gradually separates in four-sided plates.

m-*Methoxyphenoxyacetic Acid*,  .

When 2-carboxy-5-methoxyphenoxyacetic acid is heated in a sealed tube with water at 200—210° for 2 hours, decomposition takes place and on opening the tube carbon dioxide escapes. The solution, which is nearly colourless, but contains carbonaceous specks in suspension, is filtered, concentrated, and allowed to stand, when crystals gradually separate, which are purified by recrystallisation from water. On analysis:

0·1192 gave 0·2589 CO_2 and 0·0584 H_2O. C = 59·2; H = 5·4.
0·187 „ 0·4059 CO_2 „ 0·0917 H_2O. C = 59·2; H = 5·5.
$C_9H_{10}O_4$ requires C = 59·3; H = 5·5 per cent.

m-*Methoxyphenoxyacetic acid* softens at 115° and melts at 118°; it is only sparingly soluble in cold, but dissolves readily in hot, water. It has a great tendency to separate from its hot aqueous solution, on cooling, in oily drops, which take some time to solidify, but this may be avoided by keeping the solution moderately dilute and stirring continually with a glass rod on the sides of the beaker during cooling; it is then obtained in the form of slender needles.

Synthesis of m-*Methoxyphenoxyacetic Acid.*—In carrying out this synthesis, 25 grams of resorcinol monomethyl ether, $OMe{\cdot}C_6H_4{\cdot}OH$, which had been carefully freed from all traces of resorcinol by repeated fractional distillation, were dissolved in alcoholic sodium ethoxide (containing 5 grams of sodium), and the solution mixed with 35 grams of ethylic bromoacetate. On heating this mixture in a reflux apparatus on the water-bath, decomposition set in at once, and, after heating for 2 hours, water was added, the whole extracted with ether, and the ethereal solution well washed until free from alcohol, dried over calcium chloride, and evaporated. The oily residue, after twice fractionating under reduced pressure, boiled constantly at 170° (24 mm.), and gave,

on analysis, numbers which show that it consisted of pure *ethyl* m-*methoxyphenoxyacetate*, $OMe{\cdot}C_6H_4{\cdot}O{\cdot}CH_2{\cdot}CO_2Et$.

0·1545 gave 0·3545 CO_2 and 0·0946 H_2O. C = 62·6 ; H = 6·8.
$C_{11}H_{14}O_4$ requires C = 62·8 ; H = 6·7 per cent.

Hydrolysis.—When this ester (21 grams) was mixed with a filtered solution of 10 grams of potassium hydroxide in methyl alcohol, a good deal of heat was developed, and in a short time the mass became semi-solid, owing to the separation of a white, crystalline potassium salt. This was collected on the pump, washed well with methyl alcohol, and recrystallised from this solvent ; it was thus obtained in colourless needles, which are very sparingly soluble in cold methyl alcohol, but readily soluble in water. The aqueous solution of this salt gave, on acidifying, an oily precipitate which rapidly solidified, and by carefully crystallising from water, colourless needles were obtained, which were analysed, with the following results :

0·1840 gave 0·3998 CO_2 and 0·0932 H_2O. C = 59·3 ; H = 5·6.
$C_9H_{10}O_4$ requires C = 59·3 ; H = 5·5 per cent.

The m-*methoxyphenoxyacetic acid* thus obtained softened at 116° and melted at 118—119° ; it is identical with the acid obtained from the 2-carboxy-5-methoxyphenoxyacetic acid from brazilin (see above), since an intimate mixture of the two preparations melted at the same temperature as the constituents.

Brazilinic Acid, $C_{19}H_{18}O_9$, *and Brazilic Acid*, $C_{12}H_{12}O_6$.

When the chloroform extract of the acidified oxidation product of trimethylbrazilin (see p. 1405) is left for some days, it usually solidifies, but it was found impossible to obtain any crystalline products directly from it by treatment with organic solvents on account of the considerable quantity of resinous matter which it contains ; it may, however, be purified in the following way.

The resinous mass obtained from each 10 grams of trimethylbrazilin is boiled with half a litre of water, filtered from a varying quantity of insoluble tarry matter, the filtrate evaporated to about 100 c.c., and allowed to stand for 2 or 3 days. The crystals which have then separated are collected on the pump, washed with water, and dissolved in a little glacial acetic acid, from which solution the *brazilinic acid* slowly separates in hard, colourless crystals. After recrystallisation, this acid melts at 208° and gives numbers on analysis agreeing with those required for the formula $C_{19}H_{18}O_9$. It therefore contains the same number of carbon atoms as trimethylbrazilin.

0·1722 gave 0·3698 CO_2 and 0·0715 H_2O. C = 58·6 ; H = 4·6.
0·1928 „ 0·4112 CO_2 „ 0·0789 H_2O. C = 58·2 ; H = 4·6.
$C_{19}H_{18}O_9$ requires C = 58·5 ; H = 4·6 per cent.

The aqueous filtrate from the crude brazilinic acid is made slightly alkaline with sodium carbonate and evaporated to a small bulk, when, on standing, crystals of the sparingly soluble sodium salt of brazilic acid gradually separate. This salt is collected on the pump and recrystallised twice from water, from which it separates in satiny plates. It is then dissolved in water and acidified and the voluminous, needle-shaped crystals of the free acid are collected on the pump and purified by crystallisation from water. *Brazilic acid* melts at 129° and is readily soluble in hot, but only sparingly so in cold, water. On analysis :

0·1337 gave 0·2788 CO_2 and 0·0640 H_2O. C = 56·9 ; H = 5·3.
0·1431 „ 0·3003 CO_2 „ 0·0623 H_2O. C = 57·2 ; H = 4·8.
$C_{12}H_{12}O_6$ requires C = 57·2 ; H = 4·8 per cent.

The amount of brazilinic acid obtained by the oxidation of trimethylbrazilin is considerable, 1 kilo. yielding about 50 grams of the pure acid. On the other hand, brazilic acid is only produced in very small quantities, the average yield being about 7 grams from this quantity of trimethylbrazilin. Both these acids are, at the present time, being subjected to a careful examination, and it is hoped that the results which are being obtained will throw much further light on the question of the constitution of brazilin.

We wish at this stage to express our thanks to the Government Grant Committee of the Royal Society for the repeated grants which they have given us in aid of this work.

The Owens College,
Manchester.

RICHARD CLAY AND SONS, LIMITED, LONDON AND BUNGAY.

ON BRAZILIC ACID AND THE CONSTITUTION OF BRAZILIN.

BY

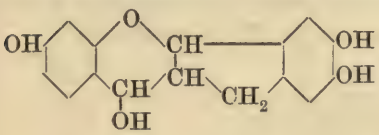
W. H. PERKIN, JUN.

From the Transactions of the Chemical Society, 1902. Vol. 81.

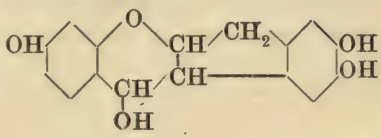
XXIII.—*On Brazilic Acid and the Constitution of Brazilin.*

By W. H. Perkin, jun.

In Part I. of this research (A. W. Gilbody, W. H. Perkin, jun., and J. Yates, Trans., 1901, 79, 1401), it was argued that since trimethylbrazilin, on oxidation with permanganate, yields 2-*carboxy*-5-*methoxyphenoxyacetic acid* and *metahemipinic acid*, the constitution of brazilin must be represented by one of the following formulæ:



I.



II.

These two formulæ are so similar that for a long time it was found impossible to obtain evidence sufficient to afford even a clue as to which was the correct one, but ultimately the detailed examination of *brazilic acid* (*loc. cit.*, p. 1410) led to results which show clearly that formula I is to be accepted as representing the constitution of brazilin.

Brazilic acid, $C_{12}H_{12}O_6$, which is produced in a yield of only 0·7 per cent. by the oxidation of trimethylbrazilin with permanganate, crystallises from water in colourless needles and melts at 129°; it is a monobasic acid, since its silver salt has the formula $C_{12}H_{11}AgO_6$, and its sodium salt the formula $C_{12}H_{11}NaO_6$; when, however, its solution in water is boiled with baryta, it yields a barium salt of the formula $C_{12}H_{10}BaO_6$, and therefore, under these circumstances, it behaves like a dibasic acid, a point which will be referred to later.

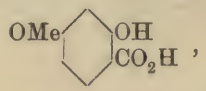
Brazilic acid contains 1 methoxy-group, as shown by Zeisel's method, and when fused with potash, it is decomposed with formation of a readily soluble acid which in aqueous solution gives an intense violet coloration with ferric chloride; it is therefore derived from the resorcyl nucleus in brazilin.

On treatment with hydroxylamine, brazilic acid yields an oxime, and with semicarbazide, a semicarbazone; it therefore contains a carbonyl group, and this group is evidently situated in the γ-position to the carboxyl group, because, when reduced with sodium amalgam, brazilic acid yields *dihydrobrazilic acid*, $C_{12}H_{14}O_6$, and this, when liberated from its sodium salt, spontaneously loses water with formation of the *lactone* $C_{12}H_{12}O_5$.

These facts, although they throw much light on the constitution of brazilic acid, are not sufficient to establish its formula, but the neces-

sary further information was ultimately obtained by the examination of the behaviour of the acid with dehydrating agents, especially sulphuric acid. When brazilic acid is warmed with concentrated sulphuric acid, it loses 1 molecule of water and is converted into *anhydrobrazilic acid*, a crystalline substance which melts at 197°, and differs sharply from brazilic acid in being very sparingly soluble even in boiling water.

This new acid is monobasic and still contains a carbonyl group, since with hydroxylamine it yields a crystalline oxime, $C_{12}H_{11}O_5N$; furthermore, a determination by Zeisel's method showed that it still contained the methoxy-group which was present in the brazilic acid. It is also an unsaturated acid, because its solution in sodium carbonate at once decolorises permanganate, and on investigating this oxidation it was found that an almost quantitative yield of p-*methoxysalicylic acid*,

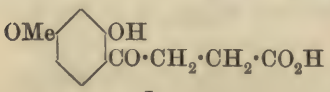


is formed if the oxidation is carried on at a sufficiently low temperature, a fact which affords a valuable clue as to the constitution of the acid.

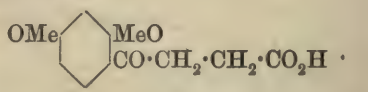
A further clue was obtained by the discovery that, when boiled with baryta water, anhydrobrazilic acid is readily decomposed into formic acid and a new acid, $C_{11}H_{12}O_5$, thus:

$$C_{12}H_{10}O_5 + 2H_2O = C_{11}H_{12}O_5 + H{\cdot}CO_2H.$$

This new acid crystallises from water in colourless needles and melts at 155°; it is a monobasic, ketonic acid and its aqueous solution gives, with ferric chloride, an intense violet coloration. Since anhydrobrazilic acid gives no coloration with ferric chloride, it was probable that the elimination of formic acid had been accompanied by the formation of a free hydroxyl group in the benzene ring. That this is the case was proved by the fact that the methyl ester of the acid $C_{11}H_{12}O_5$, when heated with sodium methoxide and methyl iodide, is converted into the methyl ester of an acid, $C_{12}H_{14}O_5$, which gives no coloration with ferric chloride; the hydroxy-group of the former acid had therefore been converted into a methoxy-group in the latter. The further consideration of the properties of the acid $C_{11}H_{12}O_5$, taken in conjunction with the fact that anhydrobrazilic acid on oxidation yields *p*-methoxysalicylic acid, seemed to indicate that the acid $C_{11}H_{12}O_5$ is 6-hydroxy-4-methoxybenzoylpropionic acid (I), and that its methyl derivative, $C_{12}H_{14}O_5$, is therefore dimethoxybenzoylpropionic acid (II),

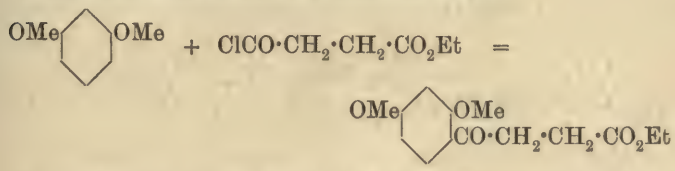


I.



II.

In order to prove this point, it was decided to attempt the synthesis of the dimethoxy-acid, and after a number of failures this was ultimately accomplished (in conjunction with Mr. E. Ormerod) by treating a mixture of dimethylresorcinol and the ester of the half-chloride of succinic acid with aluminium chloride, thus :



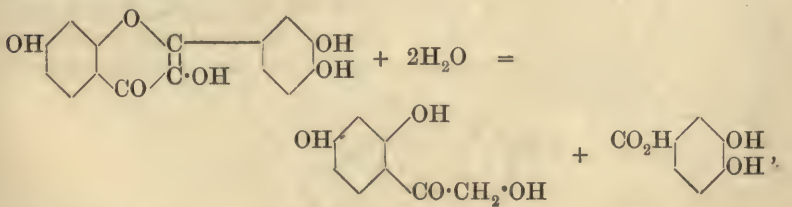
The product of this reaction yielded, on hydrolysis, an acid melting at 147°, which was identical with the dimethoxy-acid, $C_{12}H_{14}O_5$, obtained from brazilin, and the constitutions of this acid and of the hydroxymethoxy-acid, $C_{11}H_{12}O_5$, from which it was obtained are consequently proved to be represented by the formulæ II and I given above.

Referring again to the conversion of anhydrobrazilic acid by hydrolysis with baryta into hydroxymethoxybenzoylpropionic acid and formic acid,

$$C_{12}H_{10}O_5 + 2H_2O = OMe{\cdot}C_6H_3(OH){\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H + H{\cdot}CO_2H,$$

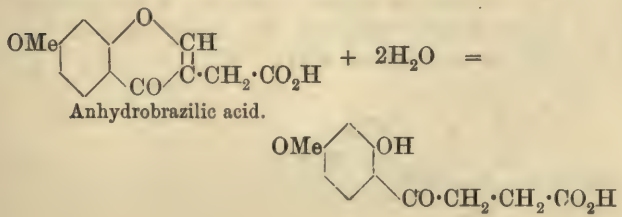
we see that we have here a case of a decomposition which has repeatedly been observed in the *pheno-γ-pyrone* series.

Thus fisetin, which is somewhat similarly constituted to brazilin, when digested with alcoholic potash is decomposed into fisetol and protocatechuic acid,



and many other similar examples might be given.

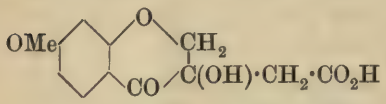
Arguing, then, from analogy, it is evident that the formula of *anhydrobrazilic acid* and its decomposition into methoxyhydroxybenzoylpropionic acid must be represented thus :



Anhydrobrazilic acid.

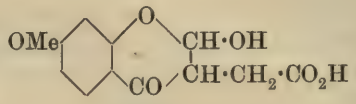
and this formula is in accordance with all the properties of the acid.

Since, then, anhydrobrazilic acid is produced from brazilic acid by the elimination of 1 molecule of water and consequent formation of a double-linking, it follows that there are only two formulæ which can represent brazilic acid, namely,



I.

and

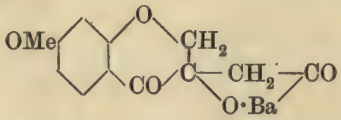


II.

In formula II, the hydroxyl group is in the γ-position in relation to the carboxyl group, and an acid of this constitution should therefore readily yield a lactone, whereas an acid, represented by formula I, being a β-hydroxy-acid, would not show any tendency to lactone formation.

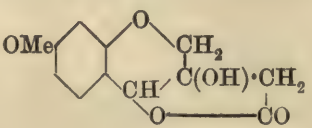
Since brazilic acid is not only stable at 100°, but even when boiled with hydrochloric acid shows no tendency to pass into a lactone, its constitution must obviously be represented by formula I.

It has been shown by the preparation and analysis of its sodium, silver, and barium salts that brazilic acid is a well-characterised, monobasic acid, but it is also pointed out (p. 228) that when boiled with baryta water it yields a very sparingly soluble barium salt of the formula $C_{12}H_{10}O_6Ba$, which is quite different from the normal salt, $(C_{12}H_{11}O_6)_2Ba$, obtained by precipitating the solution of the sodium salt with barium chloride. The formation of the salt $C_{12}H_{10}BaO_6$ is evidently due to the hydrogen of the hydroxyl group, as well as that of the carboxyl group, being replaceable by barium, that is to say, the salt has the constitution:

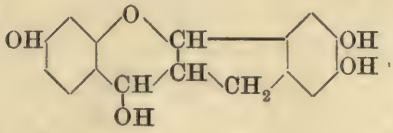


That the hydrogen of this hydroxyl group should be replaceable by treatment with caustic alkalis is not surprising in view of its proximity to the CO group of the dihydropyrone ring.

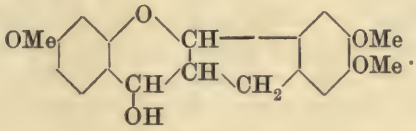
When brazilic acid is reduced by sodium amalgam, it is converted into the lactone of dihydrobrazilic acid, and the constitution of this substance must therefore be represented thus:



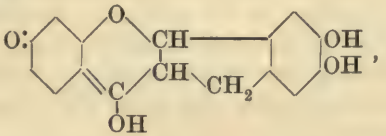
If, now, the two formulæ for brazilin given at the beginning of this paper be examined, it will be seen that only formula I can yield brazilic acid in a simple manner, and there seems, therefore, to be no reason to doubt that the constitution of brazilin is:



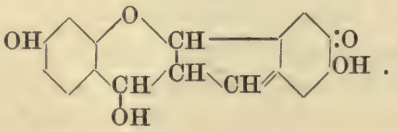
This formula accounts for all the known properties of brazilin in a satisfactory manner, and of the four hydroxyl groups three are represented as phenolic and the other one as alcoholic; it is thus obvious that three only should be converted into methoxy-groups on treating brazilin with sodium methoxide and methyl iodide, and this is actually the case. The trimethylbrazilin so produced, which has been so largely employed in this investigation, will have the constitution:



In the previous paper (*loc. cit.*, p. 1403), it was suggested that the constitution of the dye-stuff, *brazileïn*, $C_{16}H_{12}O_5$—which contains two atoms of hydrogen less than brazilin and is produced from it by oxidation—may probably be:



the two atoms of hydrogen being removed, one from the CH(OH) group and one from the OH group of the resorcyl nucleus. It must, however, be pointed out that it is quite possible that the two atoms of hydrogen may be derived from the CH_2 group and the parahydroxy-group of the catechol nucleus, and the formula of brazilein would then be:



Since, however, brazileïn yields such complicated, salt-like compounds with sulphuric acid (A. G. Perkin and Hummel, *Ber.*, 1882, 15, 2343), it

is not improbable that it may be derived from several molecules of brazilin, and therefore have a constitution much more complex than represented by the formulæ given above. This view receives some support from the fact that it has so far not been found possible to reconvert brazileïn into brazilin by reduction.

Brazilic Acid, $C_{12}H_{12}O_6$.

This acid was mentioned in the previous paper (Trans., 1901, **79**, 1411), and the method employed in isolating it from the products of the oxidation of trimethylbrazilin with potassium permanganate was briefly described. Two analyses were also given, the mean of which (C = 57·1 ; H = 5·0) agrees with the numbers required by the formula $C_{12}H_{12}O_6$ (C = 57·2 ; H = 4·8). The molecular weight of the acid has since been determined by the cryoscopic method, when two experiments gave 265 and 276, whereas the molecular weight of $C_{12}H_{12}O_6$ is 254.

Brazilic acid melts at 129—130° and is only sparingly soluble in cold water ; it dissolves readily in hot water and separates, on slowly cooling, in long, colourless needles. It dissolves readily in alcohol, ether, or acetic acid, but less readily in chloroform, and is almost insoluble in cold light petroleum ; in hot benzene, it is readily soluble, and separates, on cooling, in long needles. That brazilic acid is a saturated substance is shown by the fact that its solution in cold sodium carbonate does not decolorise permanganate, oxidation taking place, indeed, only very slowly on warming. Bromine dissolved in chloroform is also without action on the acid in the cold. An aqueous solution of brazilic acid gives no coloration with ferric chloride, but when fused with potash the acid is readily decomposed, and, on acidifying and extracting with ether, a syrupy substance is obtained which is very soluble in water and gives, with ferric chloride, an intense violet coloration.

When boiled with acetic anhydride, brazilic acid dissolves, forming a yellow solution, but this rapidly becomes brown and then quite black, decomposition evidently taking place. If a small quantity of the dry acid is heated in a test-tube, it chars and gives an oily distillate which has a strong odour of coumarin.

Brazilic acid contains one methoxy-group, as is shown by the following determinations made by Zeisel's method :

0·1429 gave 0·1370 AgI. $OCH_3 = 12·6$.
0·1892 „ 0·1795 AgI. $OCH_3 = 12·5$.
$C_{12}H_{12}O_6$, containing one OCH_3, requires $OCH_3 = 12·3$ per cent.

The residues from these methoxy-determinations were decolorised by sulphurous acid and extracted with ether, when a substance was

obtained which crystallised from water in pale yellow crystals and melted at about 178°; it was not further examined.

Salts of Brazilic Acid.—That this acid is monobasic was first proved by titration with decinormal sodium hydroxide, using phenolphthalein as the indicator.

0·21 gram, dissolved in warm water, required for neutralisation 8·1 c.c. of sodium hydroxide solution = 0·0324 gram, whereas this amount of an acid, $C_{12}H_{12}O_6$, if monobasic, would neutralise 0·033 gram NaOH.

The solution was then mixed with a further quantity of 11·9 c.c. of the sodium hydroxide (making 20 c.c. in all) and boiled for 5 minutes, when, on titrating back, it was found that the amount neutralised was practically the same as before, namely, 0·034 gram.

The *sodium* salt, $C_{12}H_{11}O_6Na$, separates in glistening plates when a hot solution of the acid is neutralised with sodium carbonate and then allowed to cool. The salt was recrystallised from water, dried at 100°, and analysed:

0·1602 gave 0·0405 Na_2SO_4. Na = 8·2.

$C_{12}H_{11}O_6Na$ requires Na = 8·4.

This salt, which does not appear to contain water of crystallisation, is comparatively sparingly soluble in cold water, although it dissolves readily on warming. On account of the facility with which it crystallises even when impure, it proved to be very valuable as a means of isolating brazilic acid from mixtures with other acids and resinous products. The corresponding potassium salt appears to be readily soluble in water.

The *silver* salt, $C_{12}H_{11}O_6Ag$, is obtained, on adding silver nitrate to a neutral solution of the ammonium salt, as a white precipitate which is very sparingly soluble in water. On analysis

0·1613 gave 0·2352 CO_2, 0·0496 H_2O, and 0·0484 Ag. C = 39·8; H = 3·4; Ag = 30·1.

0·201 gave 0·2932 CO_2, 0·0608 H_2O, and 0·0605 Ag. C = 39·8; H = 3·3; Ag = 30·1.

$C_{12}H_{11}O_6Ag$ requires C = 40·1; H = 3·1; Ag = 30·1 per cent.

The *barium* salt, $(C_{12}H_{11}O_6)_2Ba,2H_2O$.—When a neutral solution of the ammonium salt of brazilic acid is mixed with barium chloride, an amorphous, almost gelatinous, precipitate is at first produced, but this rapidly becomes crystalline. This salt is readily soluble in hot water, and separates, on cooling, in slender needles; after draining on porous porcelain and exposing to the air for 3 days, it appears to contain 2 molecules of water of crystallisation:

0·2228 air-dried salt lost, at 100°, 0·0118 = 5·3.

$(C_{12}H_{11}O_6)_2Ba,2H_2O$ requires 5·3 per cent. of water.

0·211, dried at 100°, gave 0·0773 $BaSO_4$. Ba = 21·6.

$(C_{12}H_{11}O_6)_2Ba$ requires Ba = 21·7 per cent.

A neutral solution of the ammonium salt of brazilic acid gives no precipitate with calcium chloride, a pale blue precipitate with copper sulphate, and a white, amorphous, very insoluble precipitate with lead acetate.

The *barium* salt, $C_{12}H_{10}O_6Ba$, the constitution of which is discussed in the introduction to this paper, was prepared as follows.

A hot solution of brazilic acid was rapidly mixed with a large excess of hot baryta water, when a white, granular precipitate rapidly separated and increased, apparently, on boiling. After boiling for a few minutes out of contact with air, the salt was rapidly collected on the pump, washed repeatedly with boiling water, dried at 100°, and analysed:

0·4653 gave 0·2689 $BaSO_4$. Ba = 34·0.

0·1449 „ 0·0824 $BaSO_4$. Ba = 33·5.

$C_{12}H_{10}O_6Ba$ requires Ba = 35·5.

$C_{12}H_{10}O_6Ba,H_2O$ requires Ba = 33·9 per cent.

These results, which agree better with the latter formula, clearly show that brazilic acid, when boiled with baryta, yields a dibasic barium salt. In order to be certain that no change in constitution had taken place during this treatment, the barium salt was ground in a mortar with a little dilute hydrochloric acid, and the crystalline precipitate collected on the pump, washed with water, and dried at 100°. It then melted at 129° and consisted of pure brazilic acid.

Oxime of Brazilic Acid, $C_{12}H_{13}O_6N$.—In preparing this oxime, the pure acid (0·5 gram) was dissolved in dilute caustic potash (containing 2 grams KOH), a solution of 2 grams of hydroxylamine hydrochloride was then added, and the whole allowed to stand for 24 hours. On acidifying, a flocculent precipitate separated; this was extracted with ether, the ethereal solution dried over calcium chloride and evaporated, and the syrupy residue left over sulphuric acid in a vacuum desiccator for several days, when it gradually solidified. As all attempts to recrystallise the substance were unsuccessful, it was analysed in its crude form:

0·2376 gave 12·1 c.c. nitrogen at 22° and 756 mm. N = 5·7.

$C_{12}H_{13}O_6N$ requires N = 5·3 per cent.

This oxime dissolves readily in hot water and, on cooling, separates as an oil.

Semicarbazone of Brazilic Acid, $C_{13}H_{15}O_6N_3$.—Brazilic acid appar-

ently combines with semicarbazide only with difficulty, as the following experiment shows. About 1 gram of the acid was dissolved in hot water and mixed with 1·5 grams of semicarbazide hydrochloride and 1·5 grams of sodium acetate and allowed to stand. After a few days, a thick oil had separated, which, on vigorous stirring, soon solidified to a mass of minute crystals; these appeared to consist of the semicarbazone mixed with small quantities of unchanged brazilic acid, since the substance contained only 11 per cent. of nitrogen, instead of 13·6 per cent. required by the formula $C_{13}H_{15}O_6N_3$. The filtrate from the crystals deposited, in the course of a few days, a hard, compact crust of crystals, which were collected, washed well, and dried at 100°. On analysis:

0·165 gave 18·4 c.c. nitrogen at 17° and 747 mm. N = 12·7.
$C_{13}H_{15}N_3O_6$ requires N = 13·6 per cent.

The substance began to decompose at 125—126°, then at about 150—160° it became quite solid, and a few degrees higher it again decomposed and was converted into a black mass. That this substance, although not quite pure, is the semicarbazone of brazilic acid was proved by dissolving it in hot hydrochloric acid, when, on cooling, the solution became filled with needle-shaped crystals of pure brazilic acid.

Lactone of Dihydrobrazilic Acid.

Brazilic acid is readily reduced by sodium amalgam with formation of the sodium salt of dihydrobrazilic acid, and on acidifying this the γ-hydroxy-acid at once loses water with formation of its lactone.

The pure sodium salt of brazilic acid (0·5 gram) was dissolved in water, the solution placed in a flat, porcelain dish cooled by running water, and treated with 3 per cent. sodium amalgam (100 grams) in small quantities at a time. On acidifying the product, an oily substance separated which was at first partly soluble in sodium carbonate and therefore probably contained some hydroxy-acid. In order to convert the whole into the lactone, the strongly acid liquid was warmed for a few minutes on the water-bath.

After repeatedly extracting with pure ether, the solution was dried over calcium chloride and evaporated to a small bulk, when, on standing, small, colourless, glistening crystals separated: these were collected, washed with ether, and analysed.

0·1753 gave 0·3949 CO_2 and 0·0831 H_2O. C = 61·4; H = 5·3.
0·1052 „ 0·2354 CO_2 „ 0·0498 H_2O. C = 61·0; H = 5·2.
$C_{12}H_{12}O_5$ requires C = 61·0; H = 5·1 per cent.

The *lactone* of *dihydrobrazilic acid* melts at 142—144° and is sparingly soluble in dry ether; it dissolves readily in warm water and

separates on cooling as an oil which, however, soon crystallises; it is readily soluble in alcohol, moderately so in chloroform and benzene, and sparingly soluble in light petroleum. When heated in small quantities in a test-tube, it decomposes to a large extent and gives an oily distillate smelling of coumarin; this solidifies on rubbing, and on crystallising from water some of the lactone is recovered, showing that it distils to some extent without decomposition.

The lactone dissolves in baryta water, yielding a readily soluble barium salt, but is insoluble in cold sodium carbonate; on boiling, however, it dissolves, and the solution, if well cooled and acidified, remains clear and evidently contains the hydroxy-acid, since, if heated to boiling and again cooled, the lactone separates. Concentrated sulphuric acid colours the crystals an intense crimson, and on standing a deep crimson solution is produced; this, on warming, becomes at first more intensely coloured, and then the crimson changes to dark brown.

Anhydrobrazilic Acid.

This acid is obtained when brazilic acid is treated with sulphuric acid under the following conditions. Pure brazilic acid (0·3 gram) is dissolved in 5 c.c. of sulphuric acid and the test-tube containing the solution plunged into boiling water for 1½ to 2 minutes; the dark brown solution is then cooled and mixed with 2 vols. of water when, on rubbing with a glass rod, a pale yellow, crystalline substance quickly separates. The sparingly soluble precipitate is collected on the pump, washed well, and dissolved in boiling water, a little purified animal charcoal being added, when, on cooling the filtered solution, a sandy, crystalline powder is deposited which consists of pure anhydrobrazilic acid.

In the preparation of this acid, it was found best to always work with the quantities given above; if larger quantities are used, the yield obtained is not nearly so good. From the sulphuric acid mother liquors, small quantities of the anhydro-acid mixed with some unchanged brazilic acid may be extracted with ether and the two acids may then be separated by crystallisation from water.

The total yield of anhydrobrazilic acid obtained is, however, not more than 50 per cent. of the brazilic acid used, the loss being apparently due to some of the latter acid becoming sulphonated during the process of preparation. On analysis:

0·1635 gave 0·3681 CO_2 and 0·0645 H_2O. C = 61·4; H = 4·4.
0·1472 „ 0·3319 CO_2 „ 0·0580 H_2O. C = 61·5; H = 4·4.
$C_{12}H_{10}O_5$ requires C = 61·5; H = 4·3 per cent.

Anhydrobrazilic acid is very sparingly soluble in water and melts at 197°. When heated in a test-tube, it decomposes and gives a brown

oily distillate which, on cooling, solidifies and has an odour strongly resembling that of coumarin. It dissolves readily in alcohol, but is sparingly soluble in benzene, chloroform, or ether, and almost insoluble in light petroleum. It behaves like an unsaturated acid, since its solution in sodium carbonate rapidly decolorises permanganate. That it is a monobasic acid is shown by the results obtained by titrating it with decinormal sodium hydroxide.

0·1536 required for neutralisation 0·0264 NaOH, whereas this amount of a monobasic acid, $C_{12}H_{10}O_5$, should neutralise 0·0263 NaOH.

Oxime of Anhydrobrazilic Acid, $C_{12}H_{11}NO_5$.—In preparing this oxime, a small quantity of the acid was dissolved in sodium bicarbonate, mixed with an excess of a solution of hydroxylamine hydrochloride which had been neutralised with sodium carbonate, and the whole allowed to stand for 24 hours. On acidifying, the product deposited an oil, but this rapidly solidified to a granular precipitate, which was collected, washed well, and recrystallised from boiling water. It was thus obtained as a sandy powder consisting of microscopic needles, which melted with decomposition at about 175—180°. On analysis:

0·1533 gave 0·3260 CO_2 and 0·0629 H_2O. C = 57·9; H = 4·5.
0·1567 ,, 7·9 c.c. nitrogen at 20° and 760 mm. N = 5·8.
$C_{12}H_{11}NO_5$ requires C = 57·8; H = 4·4; N = 5·6 per cent.

Oxidation of Anhydrobrazilic Acid. Formation of p-*Methoxysalicylic Acid*, $OMe{\cdot}C_6H_3(OH){\cdot}CO_2H$.—The pure acid (0·5 gram) was dissolved in dilute sodium carbonate and a cold saturated solution of permanganate added drop by drop with constant shaking until the pink colour remained permanent. After sufficient sodium sulphite had been added to destroy the excess of permanganate, the whole was boiled, filtered, and the filtrate and washings of the manganese precipitate evaporated to a small bulk. On acidifying, a colourless acid separated which crystallised from water in colourless needles. On analysis:

0·1104 gave 0·2299 CO_2 and 0·0495 H_2O. C = 56·8; H = 4·9.
$C_8H_8O_4$ requires C = 57·1; H = 4·8 per cent.

This acid melted at 156°, and its aqueous solution gave, with ferric chloride, an intense violet coloration. That it was *p*-methoxysalicylic acid was further proved by mixing it with an equal quantity of this acid, when the mixture melted at 155—156°.

6-Hydroxy-4-methoxybenzoylpropionic Acid,
$OMe{\cdot}C_6H_3(OH){\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$.

Anhydrobrazilic acid dissolves readily in warm barium hydroxide solution, and if the solution is boiled a thick, crystalline precipitate of the

barium salt of hydroxymethoxybenzoylpropionic acid rapidly forms, the separation being complete after 15 to 20 minutes.

If the solution is dilute, the separation does not take place until it is concentrated sufficiently, and then the barium salt separates in stellate groups. The barium salt is collected on the pump, washed with water, and dissolved in warm dilute hydrochloric acid, when, on standing, the free acid separates in colourless needles, and by recrystallisation from water is readily obtained pure, in long threads somewhat resembling crystals of sublimed phthalic acid. On analysis:

0·1714 gave 0·3702 CO_2 and 0·0840 H_2O. C = 58·9; H = 5·4.
0·1541 „ 0·3329 CO_2 „ 0·0756 H_2O. C = 58·9; H = 5·4.
$C_{11}H_{12}O_5$ requires C = 58·9; H = 5·3 per cent.

6-Hydroxy-4-methoxybenzoylpropionic acid melts at 155—156° and dissolves readily in hot, but is rather sparingly soluble in cold, water; its aqueous solution gives an intense violet coloration with ferric chloride.

The *barium* salt, obtained by the action of barium hydroxide on anhydrobrazilic acid in the way described above, after drying at 100°, was analysed with the following results:

0·3987 gave 0·2440 $BaSO_4$. Ba = 36·1.
$C_{11}H_{10}O_5Ba,H_2O$ requires Ba = 36·4 per cent.

From this it would appear that the barium salt prepared in this way has the formula $C_{11}H_{10}O_5Ba,H_2O$, that is to say, that the barium has replaced, not only the hydrogen of the carboxyl group, but also that of the phenolic hydroxyl group.

Such cases as this have often been observed before; thus salicylic acid yields a barium salt, $C_7H_4O_3Ba,2H_2O$, which is very sparingly soluble in water.

The filtrates from several preparations of the barium salt of hydroxymethoxybenzoylpropionic acid were mixed and the excess of barium hydroxide removed by passing carbon dioxide through the boiling solution.

The filtrate deposited, on evaporation, a further small quantity of the insoluble barium salt; this was removed by filtration, and the concentrated solution, which contained a considerable quantity of a barium salt, carefully tested for formic acid. This was easily proved to be present, not only by the fact that the solution blackened silver nitrate, but also because it readily reduced mercuric chloride to mercurous chloride. There can, therefore, be no doubt that anhydrobrazilic acid is decomposed by boiling with barium hydroxide into formic acid and hydroxymethoxybenzoylpropionic acid, according to the equation

$$C_{12}H_{10}O_5 + 2H_2O = H{\cdot}CO_2H + C_{11}H_{12}O_5.$$

Dimethoxybenzoylpropionic Acid, $C_6H_3(OMe)_2 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CO_2H$.

It was necessary to prepare this acid, in order to compare it with the acid obtained synthetically by the action of aluminium chloride on the mixture of dimethylresorcinol and the ester of the half-chloride of succinic acid (see next section).

Hydroxymethoxybenzoylpropionic acid (1 gram) was dissolved in 12 grams of methyl alcohol, 3 grams of concentrated sulphuric acid added, and the whole heated to boiling in a reflux apparatus for 4 hours.

On adding water, a crystalline substance separated, which, since it was insoluble in sodium carbonate, evidently consisted of the methyl ester, $OMe \cdot C_6H_3(OH) \cdot CO \cdot CH_2 \cdot CH_2 \cdot CO_2Me$. In this condition, it melted at about 85°, and its alcoholic solution gave an intense violet with ferric chloride; it was, however, not further purified, owing to the necessity for using the whole quantity for further methylation. The dry methyl ester (0·8 gram) was dissolved in dilute sodium methoxide (containing 0·1 gram Na) and heated in a sealed tube with 3 grams of methyl iodide at 120° for 2 hours; the tube was then opened, the same quantity of sodium methoxide and methyl iodide again added, the tube resealed, and heated at 120—130° for 3 hours. The product was poured into water, the oily precipitate extracted with ether, the ethereal solution well washed with water, and then three times with dilute soda in order to extract some unmethylated ester which was present. The ethereal solution was then evaporated and the residual oil hydrolysed by boiling for a few minutes with methyl alcoholic potash. Water was then added and the clear solution evaporated until free from methyl alcohol, when, on the addition of hydrochloric acid, a crystalline acid was deposited, which was collected, washed with water, dried on a porous tile, and recrystallised twice from benzene. On analysis:

0·1250 gave 0·2779 CO_2 and 0·0673 H_2O. C = 60·6; H = 6·0.

$C_{12}H_{14}O_5$ requires C = 60·5; H = 5·9 per cent.

Dimethoxybenzoylpropionic acid melts at 146—148°, with slight previous softening, and when kept a short time a few degrees above its melting point, it becomes a deep violet colour. It is readily soluble in alcohol and in hot benzene, but sparingly so in cold benzene; its alcoholic solution gives no coloration with ferric chloride.

Synthesis of Dimethoxybenzoylpropionic Acid.

[With E. Ormerod.]

In synthesising this acid, a process was employed which is somewhat similar to that recommended by L. Bouveault (*Bull. Soc. Chim.*, 1897, [iii], **17**, 333) as suitable for cases of this kind.

Dimethylresorcinol (8·4 grams) was dissolved in nitrobenzene (17 grams) and carbon disulphide (35 grams), and then mixed with the ester of the half-chloride of succinic acid, $Cl{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2Et$ (10 grams). Powdered aluminium chloride* (8 grams) was then added in small quantities and, after standing for some hours, the mixture was gently heated on the water-bath for a few minutes.

The product was treated with water, the oily layer well washed with water, and the carbon disulphide removed on the water-bath; the residue was then distilled in steam until the nitrobenzene and small quantities of unchanged dimethylresorcinol had been removed. The non-volatile oil was extracted with ether, the ethereal solution evaporated, and the brown oil hydrolysed with a slight excess of alcoholic potash. After evaporating off the alcohol, the residue was dissolved in water and acidified, when a brown solid separated, which was collected on the pump and purified by repeated recrystallisation from benzene. On analysis:

0·1559 gave 0·3465 CO_2 and 0·0834 H_2O. C = 60·6; H = 5·9.

$C_{12}H_{14}O_5$ requires C = 60·5; H = 5·9 per cent.

The synthetical dimethoxybenzoylpropionic acid thus obtained melted at 146—148° with slight previous softening, and the melted mass became a deep violet colour a few degrees above this temperature. That it is identical with the acid of this composition obtained from anhydrobrazilic acid as described above, was further proved by mixing the two acids, when no alteration in the melting point could be observed.

In conclusion, I wish to express my thanks to Mr. J. Yates for his valuable assistance in carrying out this investigation, and I wish also to state that much of the expense incurred was defrayed by repeated grants from the Royal Society Fund.

The Owens College,
Manchester.

* Prepared from aluminium.

RICHARD CLAY AND SONS, LIMITED, LONDON AND BUNGAY.

BRAZILIN AND HÆMATOXYLIN. PART III. THE CONSTITUTION OF HÆMATOXYLIN.

BY

W. H. PERKIN, JUN.,

AND

J. YATES.

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XXIV.—*Brazilin and Hæmatoxylin. Part III. The Constitution of Hæmatoxylin.*

By W. H. Perkin, jun., and J. Yates.

Hæmatoxylin is the colouring matter of *Hæmatoxylon campechianum*, a tree which belongs to the family *Cæsalpiniaceæ*, and the wood of which appears to have been first imported into Europe by the Spaniards shortly after the discovery of America. The heart-wood of this tree, known as logwood in this country, is still largely used in cotton and wool dyeing for the production of blacks and greys, and it is also employed on account of its cheapness along with other colours, such as indigo, for dyeing compound shades.

The importance of hæmatoxylin may be judged from the fact that it has probably been, and perhaps is still, more largely used than any other natural colouring matter, not even excepting indigo. The dye is sent into the market either as a concentrated liquid extract or in the solid form, the rasped wood, in either case, being extracted with water and the extract evaporated in vacuum pans.

For dyeing cotton, or in calico printing, logwood extract is generally used in conjunction with an iron, chromium, or aluminium mordant; the two first-named give intense black, whereas, with the latter, greyish-violet shades are produced. Very large quantities of the liquid extract are still used in wool dyeing for the production of blacks, the wool being immersed alternately in the extract, and in a bath of potassium dichromate and sulphuric acid. Again, in silk dyeing, logwood extract is very largely used in conjunction with an iron mordant for the production of blacks. It is worthy of note that hæmatoxylin and iron alum have long been used as one of the most important stains for microscopical sections of animal tissues, but, quite recently, Professor S. J. Hickson (*Quart. J. Micros. Sci.*, 1901, p. 469) has shown that brazilin used with iron alum gives results which are even more satisfactory.

The actual colouring matter of logwood was first isolated by Chevreul (*Ann. Chim. Phys.*, [ii], 82, 53, 126) in 1810, who obtained it by extracting the wood with water, evaporating the extract to dryness, and digesting the residue with alcohol, which dissolved the hæmatoxylin, but not the other substances present.

After distilling off the alcohol, the residue was allowed to stand in contact with water, when the hæmatoxylin separated in crystals. Pure hæmatoxylin is now comparatively easily obtained from the dark coloured crusts which gradually separate when the casks of concentrated logwood extract are allowed to stand in a cool place. The crude mass

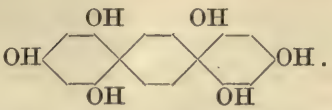
is ground to a fine powder, extracted repeatedly with ether, the ethereal solution evaporated, and the residue left in contact with water when dark coloured crystals separate, which, by recrystallisation from water containing a small quantity of sodium bisulphite, may be obtained colourless, and consist then of pure hæmatoxylin.

Hæmatoxylin crystallises in tetragonal prisms with 3 molecules of water of crystallisation, and is sparingly soluble in cold, but readily in hot, water; it dissolves in alkalis, forming an intense purple-coloured solution. It is strongly dextrorotatory, a 1 per cent. aqueous solution having a rotation of 1·85° in a 200 mm. tube; it also reduces Fehling's solution and silver nitrate in the cold.

The first attempt to determine the composition of hæmatoxylin is due to Erdmann, who in 1842 (*Annalen*, 44, 292) proposed the formula $C_{40}H_{17}O_5$; this he subsequently altered to $C_{16}H_{14}O_6$, for the anhydrous substance and this formula, which was confirmed by Hesse (*Annalen*, 1859, 109, 332) and by other workers, is now accepted as correct.

From very early times experiments were made with the object of obtaining evidence as to the nature of this important dye-stuff, but the results in most cases did not afford any clue to its constitution. The literature bearing on the subject is, in fact, so extended, that it is only possible in this paper to give a very brief outline of such of the work as produced really valuable evidence of the nature of hæmatoxylin.

Reim (*Ber.*, 1871, 4, 331) showed that when an ethereal solution of hæmatoxylin is mixed with a few drops of nitric acid, oxidation takes place and hæmateïn, $C_{16}H_{12}O_6$, is produced. J. J. Hummel and A. G. Perkin (*Ber.*, 1882, 15, 2337) subsequently obtained hæmateïn pure in the form of reddish-brown crystals by leading air through a solution of the dye-stuff in ammonia. The action of fused caustic potash on hæmatoxylin was also first investigated by Reim (*loc. cit.*, 332) and from the fused mass he was able to isolate considerable quantities of *pyrogallol*, a result of great importance, since it showed that hæmatoxylin is probably a derivative of this substance. R. Meyer (*Ber.*, 1879, 12, 1392) submitted hæmatoxylin to dry distillation, and obtained a distillate which he stated contained resorcinol, as well as pyrogallol, but the qualitative tests by which he claimed to have recognised the former of these were quite insufficient, and it will be shown in this paper that resorcinol is not formed in this way. That hæmatoxylin contains several hydroxyl groups was clear from early times, and in order to determine how many such groups were present in the molecule, Reim (*loc. cit.*, 331) investigated its behaviour with acetyl chloride, and obtained a substance which he considered to be hexa-acetylhæmatoxylin, $C_{16}H_8O_6(C_2H_3O)_6$, and as a result of this he suggested the first constitutional formula for hæmatoxylin, namely,



Erdmann and Schultz (*Annalen*, 1883, 216, 234), by determining the number of acetyl groups in this substance, subsequently showed that Reim's substance was *penta-acetylhæmatoxylin* and had the formula $C_{16}H_9(C_2H_3O)_5O_6$, and therefore hæmatoxylin contains only five hydroxyl groups. This result was confirmed by the investigation of the action of sodium methoxide and methyl iodide on hæmatoxylin when, under certain conditions (Herzig, *Monatsh.*, 1894, 15, 143), tetramethylhæmatoxylin, $C_{16}H_{10}O_2(OMe)_4$, is produced a substance which still contains a hydroxyl group, since on treatment with acetic anhydride it yields acetyltetramethylhæmatoxylin,

$$C_{16}H_9O(OMe)_4 \cdot OC_2H_3O.$$

It is thus shown that hæmatoxylin, like brazilin, contains an alcoholic hydroxyl group which is not methylated by the action of sodium methoxide and methyl iodide, and indeed, from the general similarity between brazilin and hæmatoxylin, it has long been considered probable that these two colouring matters are closely allied in constitution.

During the investigation of brazilin, we have also carried out a number of experiments on hæmatoxylin, the results of which, in our opinion, not only prove the close relationship of these two colouring matters, but also enable us to assign a formula to hæmatoxylin which we believe correctly represents the constitution of this substance.

In the present paper, we describe only the experiments on the oxidation of tetramethylhæmatoxylin with permanganate, and leave for a future communication the description of the interesting substances which have been obtained by oxidising tetramethylhæmatoxylin with chromic acid.

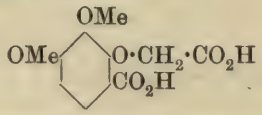
We have also carefully repeated R. Meyer's (*loc. cit.*) experiments on the distillation of hæmatoxylin, and show that pyrogallol (but no resorcinol) is produced in considerable quantity in this way. We are thus able to confirm Reims' discovery (*loc. cit.*) that hæmatoxylin is probably a derivative of pyrogallol.

When tetramethylhæmatoxylin is oxidised with permanganate, it yields m-*hemipinic acid*, an important result, because it shows that hæmatoxylin, like brazilin, contains the catechol nucleus. Briefly stated, then, the molecule of brazilin is made up of a resorcinol and a catechol nucleus, whereas hæmatoxylin contains a pyrogallol and a catechol nucleus.

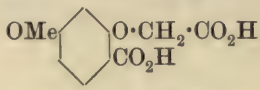
From the product of the oxidation of tetramethylhæmatoxylin, we

have also been able to isolate considerable quantities of a beautifully crystalline acid, $C_{11}H_{12}O_7$, which melts at 215°.

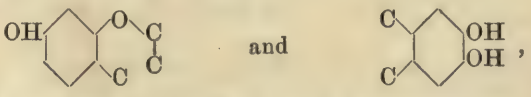
This acid is dibasic, since it yields a silver salt, $C_{11}H_{10}O_7Ag_2$; it is also converted into the anhydride $C_{11}H_{10}O_6$ by treatment with acetic anhydride, and as it contains two methoxy-groups and yields pyrogallol when heated in a sealed tube with hydrochloric acid, its constitution is evidently represented by the formula:



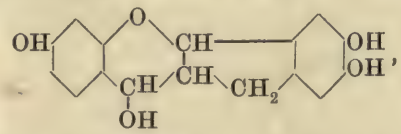
that is to say, it is 2-*carboxy*-5 : 6-*dimethoxyphenoxyacetic acid*. This acid is therefore exactly similar to the 2-*carboxy*-5-*methoxyphenoxyacetic acid*:



which was obtained from trimethylbrazilin by oxidation with permanganate, from which, indeed, it only differs by containing an extra methoxy-group. The close relationship between brazilin and hæmatoxylin which owing to the general similarity in the properties of these two colouring matters has so long been considered probable, is now clearly proved and may be briefly expressed in the following way. Trimethylbrazilin, on oxidation, yields 2-carboxy-5-methoxyphenoxyacetic acid and *m*-hemipinic acid, and therefore its constitutional formula must contain the two nuclei:

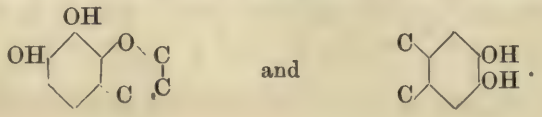


These two combined together lead, then, to the formula,

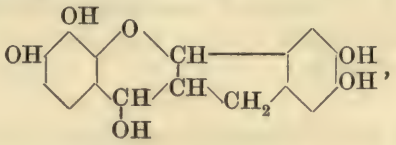


which, as shown in the preceding paper, there is every reason to believe represents the constitution of brazilin.

Similarly, tetramethylhæmatoxylin, on oxidation with permanganate, yields 2-carboxy-5 : 6-dimethoxyphenoxyacetic acid and *m*-hemipinic acid, and therefore hæmatoxylin must contain the two nuclei:



These combined together in the same way as in the construction of the brazilin formula give the expression



as representing the constitution of hæmatoxylin, and as this accounts in a satisfactory manner for all the known decompositions of this colouring matter, there can be little doubt that it is correct.

Besides the acids mentioned above, another acid is formed in the oxidation of tetramethylhæmatoxylin with permanganate in considerable quantities; this melts at 180°, has the formula $C_{20}H_{20}O_{10}$, and has been named *hæmatoxylinic acid.*

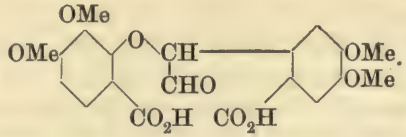
This new acid, which it will be seen contains the same number of carbon atoms as tetramethylhæmatoxylin, is dibasic, since its silver salt has the composition $C_{20}H_{18}Ag_2O_{10}$.

On reduction with sodium amalgam, it is converted quantitatively into an acid, $C_{20}H_{20}O_9$, which is a monobasic lactonic acid, and it is therefore evident that the latter is produced in two stages, thus:

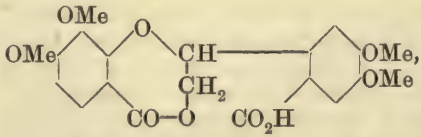
$$\underset{\text{Hæmatoxylinic acid.}}{C_{20}H_{20}O_{10}} + 2H = \underset{\text{Dihydrohæmatoxylinic acid.}}{C_{20}H_{22}O_{10}}$$

$$C_{20}H_{22}O_{11} - H_2O = \underset{\text{Lactone of dihydrohæmatoxylinic acid.}}{C_{20}H_{20}O_9}$$

Hæmatoxylinic acid corresponds in all its properties with brazilinic acid, $C_{19}H_{18}O_9$ (Trans., 1901, 79, 1411), from which it differs only by one methoxy-group, and it is extremely probable that its constitution is:



The lactone of dihydrohæmatoxylinic acid would then be



or the CO_2H of the catechol nucleus might of course take part in the

lactone formation. To prove conclusively the constitutions of brazilinic and hæmatoxylinic acids is a matter of great difficulty, and a description of the large amount of experimental work which has been accumulated with this object will, it is hoped, form the subject matter of a future communication.

Oxidation of Tetramethylhæmatoxylin with Permanganate.*

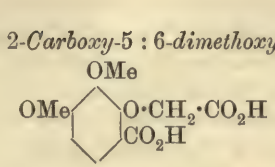
This oxidation, like the oxidation of trimethylbrazilin, was carried out under a variety of conditions, but the following method was the one ultimately adopted in preparing the substances described in this paper.

Tetramethylhæmatoxylin (10 grams) is ground up with a little water into the finest possible paste, washed into a three litre flask with 100 c.c. of water, and then 100 c.c. of a cold saturated solution of permanganate added and the whole allowed to stand at the ordinary temperature until the colour has disappeared. A further 100 c.c. of permanganate are then added, and the operation continued until, after standing for 10—12 hours, the liquid still remains pink. The excess of permanganate is then destroyed by adding sodium sulphite and the product, after heating to boiling, filtered on the pump; the maganese precipitate is then extracted twice with boiling water and the combined aqueous solutions nearly neutralised with hydrochloric acid and evaporated to a small bulk, but not to dryness.

On acidifying the residue with hydrochloric acid, a small quantity of a black, tarry substance separates and is removed by filtration, the red fitrate is then shaken with chloroform, which causes a small quantity of a crystalline substance (A) to separate; the filtrate from this is then repeatedly extracted with chloroform. The chloroform extract is washed with a little water, dried over calcium chloride, when, on distilling off the chloroform, a semi-solid tarry mass remains (B). The solution, after treatment with chloroform, is saturated with ammonium sulphate and extracted at least 10 times with ether; the ethereal solution is dried over calcium chloride and evaporated and in this way a brick-red, crystalline mass is obtained (C).

* The hæmatoxylin used in this research was obtained from Kahlbaum and was always of excellent quality. The preparation of the tetramethylhæmatoxylin was carried out almost exactly in the way described in the case of trimethylbrazilin (Trans., 1901, **79**, 1403). On pouring the product of methylation into water and allowing the whole to stand for a few days, in almost all cases, part of the tetramethylhæmatoxylin separated in roseate groups of straw-coloured needles; these melted at 65—70° and contained water of crystallisation. After drying at 100° and recrystallising from alcohol, the substance was obtained in an anhydrous condition melting at 140—142°. The rest of the tetramethylhæmatoxylin was extracted with ether and purified as in the case of the trimethylbrazilin: but in the oxidation experiments, much better results were always obtained with the crystals melting at 65—70° than with the anhydrous substance.

The Substance A is 2-Carboxy-5 : 6-dimethoxyphenoxyacetic Acid,



The substance A crystallises from glacial acetic acid in colourless needles and so easily that even when much contaminated with resin, as was frequently the case, it separates at once from this solvent in an almost pure condition. After two crystallisations, the following numbers were obtained on analysis :

0·1730 gave 0·3258 CO_2 and 0·0753 H_2O. C = 51·4 ; H = 4·8.
0·1153 „ 0·2179 CO_2 „ 0·0495 H_2O. C = 51·5 ; H = 4·8.
$C_{11}H_{12}O_7$ requires C = 51·6 ; H = 4·7 per cent.

2-Carboxy-5 : 6-dimethoxyphenoxyacetic acid melts at 214—215° and at about 225—230° decomposes with evolution of gas. It is almost insoluble in cold water, but is dissolved slightly by boiling water and is deposited on cooling in needles ; it is sparingly soluble in cold acetic acid, but dissolves readily on boiling.

The methoxy-groups were determined by Zeisel's method :

0·2703 gave 0·5148 AgI. MeO = 25·2.
$CO_2H{\cdot}C_6H_2(MeO)_2O{\cdot}CH_2{\cdot}CO_2H$ requires MeO = 24·2 per cent.

The silver salt, $C_{11}H_{10}O_7Ag_2$, is precipitated on the addition of silver nitrate to a neutral solution of the ammonium salt as a white, gelatinous precipitate which is difficult to wash. On analysis :

0·2251 gave 0·2343 CO_2, 0·0457 H_2O, and 0·1035 Ag. C = 28·3 ; H = 2·2 ; Ag = 46·0.
$C_{11}H_{10}O_7Ag_2$ requires C = 28·1 ; H = 2·1 ; Ag = 45·9 per cent.

A neutral solution of the ammonium salt gives a white, gelatinous precipitate with calcium chloride, but with barium chloride no precipitate is produced until the solution is boiled, and then a very sparingly soluble, crystalline salt separates. When fused with potash, the acid gives a brown mass, and the solid acid obtained from this by acidifying and extracting with ether gives all the reactions of pyrogallol.

In order to clearly prove that this acid is a derivative of pyrogallol, a small quantity was heated with hydrochloric acid in a sealed tube for 2 hours at 180°. On opening the tube, carbon dioxide escaped, and the liquid contained small, black flocks in suspension ; these were removed by filtration. The filtrate was saturated with ammonium sulphate, extracted five times with ether, and the ethereal solution, after drying with calcium chloride, evaporated, when a brown oil remained

which was distilled under reduced pressure from a small retort. The distillate, which was a light brown oil, crystallised at once on rubbing with a trace of pyrogallol, and, in contact with porous porcelain, the dark mother liquor was rapidly absorbed, leaving a colourless, crystalline residue. After crystallising from benzene, this melted at 125—130°, gave with ferric chloride a blue colour rapidly changing to brownish-green, and with nitrous acid a yellow colour changing to brown, and since when dissolved in potash and left exposed to air a deep brown solution was obtained, there can be no doubt that the substance is pyrogallol (m. p. 132°).

Anhydride of Carboxydimethoxyphenoxyacetic Acid.

When this acid is heated in a small flask under reduced pressure, it first melts, then water is eliminated, and an oily distillate is obtained which has a penetrating odour like that of formaldehyde, and which, on cooling and rubbing, partly solidifies. When this was ground up with ether, some dissolved, but a portion remained insoluble as a white, crystalline powder which softened at 150° and melted at 175°. This substance dissolved only partly in cold dilute sodium carbonate, and the solution, on acidifying, deposited a considerable quantity of the unchanged acid melting at 214°. The residue consisted of the crude anhydride of the acid.

It appears, therefore, that on distillation under reduced pressure the acid is partly converted into the anhydride and partly distils unchanged.

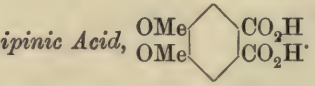
Subsequently, the pure anhydride was obtained by heating the acid in a reflux apparatus with acetic anhydride for 20 minutes. The solution, on standing over potash in a vacuum desiccator, gradually deposited square plates from which, after drying at 100°, the following numbers were obtained on analysis:

0·1488 gave 0·3013 CO_2 and 0·0575 H_2O. C = 55·2; H = 4·3.

$C_{11}H_{10}O_6$ requires C = 55·4; H = 4·2 per cent.

This substance is therefore the *anhydride of carboxydimethoxyphenoxyacetic acid.*

The Substance C is Metahemipinic Acid,



The substance C, obtained from the ethereal extract (p. 240) of the product of the oxidation of trimethylhæmatoxylin with permanganate, was a brick-red powder sparingly soluble in ether. In purifying it, it was first washed on the pump with ether and then crystallised from water with the aid of animal charcoal, and was thus obtained in almost

colourless, glistening needles which melted at 190° with decomposition and consisted of pure m-*hemipinic acid*. On analysis:

0·1284 gave 0·2496 CO_2 and 0·0529 H_2O. C = 53·0; H = 4·6.
$C_{10}H_{10}O_6$ requires C = 53·1; H = 4·4 per cent.

As it was most important to be certain of the identity of this acid, it was next converted into the silver salt, which was obtained as a granular precipitate on adding silver nitrate to a neutral solution of the ammonium salt. On analysis:

0·1489 gave 0·1517 CO_2, 0·0279 H_2O, and 0·0728 Ag. C = 27·7; H = 2·1; Ag = 48·8.
$C_{10}H_8O_6Ag_2$ requires C = 27·3; H = 1·9; Ag = 49·1 per cent.

Lastly, the characteristic ethylimide was prepared by dissolving the acid in ethylamine, evaporating to dryness, distilling the residue, and crystallising the distillate from alcohol. The yellow needles which separated melted at 230° and consisted of pure *m*-hemipinethylimide. On analysis:

0·1829 gave 9·6 c.c. of nitrogen at 13° and 732 mm. N = 6·2.
$C_{12}H_{13}O_4N$ requires N = 5·9 per cent.

There can therefore be no doubt that the acid is *m*-hemipinic acid, a very important fact, since it proves that hæmatoxylin contains the catechol nucleus.

Hæmatoxylinic Acid, $C_{20}H_{20}O_{10}$.

This acid is contained in the chloroform extract (B) of the product of the oxidation of tetramethylhæmatoxylin, and is evidently that derivative of hæmatoxylin which corresponds with brazilinic acid (Trans., 1901, **79**, 1411) obtained in a similar way from trimethylbrazilin. The tarry residue left after distilling off the chloroform was boiled with a large quantity of water, when all dissolved except a small quantity of dark coloured, resinous matter. The aqueous solution was mixed with an excess of basic lead acetate, and the pale yellow, amorphous precipitate which separated was collected and well washed with water. The precipitate was then ground up with water to a fine paste and decomposed with sulphuretted hydrogen, first by passing the gas in the cold, and afterwards through the boiling liquid. After filtering, the precipitate was again heated with water and sulphuretted hydrogen, and the combined, nearly colourless filtrates were then evaporated to a small bulk. The concentrated aqueous solution, on standing, deposited nodular crystals; these were collected, washed with water, and recrystallised from glacial acetic

acid, from which the new acid separated in colourless needles. On analysis:

0·1717 gave 0·3582 CO_2 and 0·0714 H_2O. C = 56·9; H = 4·6.
0·1546 „ 0·3231 CO_2 „ 0·0677 H_2O. C = 57·0; H = 4·8.
$C_{20}H_{20}O_{10}$ requires C = 57·1; H = 4·8 per cent.

Hæmatoxylinic acid melts at 180° without decomposition, and is very sparingly soluble in water; it dissolves readily in hot methyl alcohol and glacial acetic acid, but is sparingly soluble in chloroform, very sparingly so in benzene, and almost insoluble in light petroleum.

Hæmatoxylinic acid, like brazilinic acid, dissolves in concentrated sulphuric acid, producing an intense reddish-brown solution. That it is a dibasic acid is shown by the following results, obtained by titrating with decinormal sodium hydroxide.

0·2067 neutralised 0·041 gram NaOH, whereas this amount of a dibasic acid of the formula $C_{20}H_{20}O_{10}$ should neutralise 0·04 gram NaOH.

Salts of Hæmatoxylinic Acid.—The silver salt, $C_{20}H_{18}O_{10}Ag_2$, is obtained as a white, granular precipitate on adding silver nitrate to a neutral solution of the ammonium salt. On analysis:

0·2201 gave 0·3030 CO_2, 0·0549 H_2O, and 0·0704 Ag. C = 37·6; H = 2·8; Ag = 33·6.
$C_{20}H_{18}O_{10}Ag_2$ requires C = 37·8; H = 2·8; Ag = 34·0 per cent.

The neutral solution of the ammonium salt gives no precipitate with calcium chloride, barium chloride, or zinc sulphate, but on the addition of copper sulphate a pale green, very sparingly soluble salt separates.

Lactone of Dihydrohæmatoxylinic Acid, $C_{20}H_{20}O_9$.

This lactone acid is formed by the action of sodium amalgam on hæmatoxylinic acid, reduction and elimination of water taking place simultaneously, as explained in the introduction (p. 239).

In preparing the lactone acid, pure hæmatoxylinic acid was dissolved in dilute caustic soda and left in contact with excess of 3 per cent. sodium amalgam for 24 hours. On acidifying the strongly alkaline solution, a gelatinous precipitate separated, which was collected on the pump, washed with water, and purified by recrystallisation from glacial acetic acid, from which it separated in beautiful, colourless needles. On analysis:

0·1748 gave 0·377 CO_2 and 0·0759 H_2O. C = 58·8; H = 4·8.
0·1380 „ 0·2996 CO_2 „ 0·0621 H_2O. C = 59·2; H = 4·9.
$C_{20}H_{20}O_9$ requires C = 59·4; H = 4·9 per cent.

The *lactone* of *dihydrohæmatoxylinic acid* melts at 192—193° without decomposition, and is practically insoluble in cold water; it dis-

solves, however, slightly in boiling water, and the solution, on cooling, deposits the acid in the form of peculiar gelatinous flocks. It is moderately readily soluble in hot methyl alcohol, and separates on cooling in microscopic needles resembling asbestos threads; it is readily soluble in hot glacial acetic acid, but almost insoluble in chloroform, benzene, and light petroleum. Concentrated sulphuric acid colours the crystals a salmon-pink,* and on standing a pink solution is formed, the colour of which becomes more intense on warming, and the solution on diluting with water deposits a white, amorphous precipitate.

That this new acid is a lactonic acid is shown by the following titration experiments:

I. 0·229 gram of substance, titrated with decinormal sodium hydroxide in the cold, neutralised 0·0234 gram NaOH, whereas this amount of a *monobasic* acid, $C_{20}H_{20}O_9$, should neutralise 0·0227 gram NaOH.

II. 0·2357 gram was boiled with excess of decinormal sodium hydroxide for 10 minutes and the excess determined by titration with decinormal sulphuric acid. It was found that 0·0478 gram NaOH had been neutralised, whereas, on the assumption that the lactone ring had been hydrolysed and the acid become *dibasic*, the amount of substance taken should have neutralised 0·0467 gram NaOH.

Salts of the Lactone of Dihydrohæmatoxylinic Acid.—The silver salt, $C_{20}H_{19}O_9Ag$, was prepared by adding silver nitrate to a neutral solution of the ammonium salt. It is a white, amorphous precipitate very sparingly soluble in water. On analysis:

0·1640 gave 0·2789 CO_2, 0·0557 H_2O, and 0·0342 Ag. C = 46·4 H = 3·8; Ag = 20·9.

$C_{20}H_{19}O_9Ag$ requires C = 46·9; H = 3·7; Ag = 21·1 per cent.

The neutral solution of the ammonium salt gives no precipitate with barium or calcium chlorides, even on boiling; copper sulphate gives a pale blue, very insoluble precipitate, and zinc sulphate a white, caseous salt which melts in boiling water.

Distillation of Hæmatoxylin.

[With A. W. Gilbody.]

It was pointed out in the introduction (p. 237) that our results showed that hæmatoxylin must contain a pyrogallol and a catechol nucleus, and that the statement of R. Meyer (*Ber.*, 1889, **12**, 1392), that this substance, on distillation, yields pyrogallol and *resorcinol*, was

* This colour reaction is much less intense than that shown in the case of the corresponding lactone of dihydrobrazilinic acid, a substance which will be described in a future communication.

not in harmony with our work, and we therefore felt it necessary to repeat his experiments. In doing this, hæmatoxylin (10 grams) was distilled from a small retort under reduced pressure, and the brown, semi-solid distillate from ten such experiments was dissolved in water and filtered from a small quantity of insoluble resinous matter. The solution, which reacted strongly acid, was precipitated with excess of lead acetate and the voluminous lead salt, after washing with water, suspended in water and decomposed by sulphuretted hydrogen. The filtrate from the lead sulphide deposited, on evaporation, a brown, semi-solid mass, which was repeatedly extracted with hot benzene, when, on concentrating the benzene solution and allowing it to stand, a mass of crystals of nearly pure pyrogallol separated. After recrystallising from toluene with the aid of animal charcoal, the following results were obtained on analysis :

0·2046 gave 0·4274 CO_2 and 0·0878 H_2O. C = 57·0 ; H = 4·8.
$C_6H_3(OH)_3$ requires C = 57·1 : H = 4·8 per cent.

The substance melted at 130—131° and showed all the reactions of pyrogallol. The filtrate from the lead salt, which should contain any resorcinol which had been formed, was acidified with sulphuric acid and extracted five times with ether. The ethereal solution was washed with dilute sodium hydrogen carbonate, dried over calcium chloride, and evaporated, when only a small quantity of a dark-coloured oil remained, which was found to contain traces of pyrogallol which had escaped precipitation by the lead acetate. We were not able, in spite of every careful experiments, to detect even a trace of resorcinol in this oil, and therefore conclude that the statement that resorcinol is formed by the distillation of hæmatoxylin is incorrect.

We wish to state that much of the expense which was incurred during this long investigation has been met by repeated grants from the Government Grant Fund of the Royal Society.

The Owens College,
Manchester.

RICHARD CLAY AND SONS, LIMITED, LONDON AND BUNGAY.

BRAZILIN AND HÆMATOXYLIN. PART IV. ON DIMETHOXYCARBOXYBENZOYLFORMIC ACID, BRAZILINIC ACID, ETC.

BY

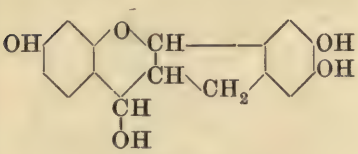
W. H. PERKIN, JUN.

From the Transactions of the Chemical Society, 1902. Vol. 81.

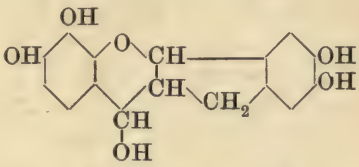
CV.—*Brazilin and Hæmatoxylin. Part IV. On Dimethoxycarboxybenzoylformic Acid, Brazilinic Acid, &c.*

By W. H. Perkin, jun.

In the first three parts of this investigation (Trans., 1901, **79**, 1397; this vol., 221, 236), experiments were described the results of which appeared to the author to prove that the constitutions of brazilin and hæmatoxylin were best represented by the two formulæ;

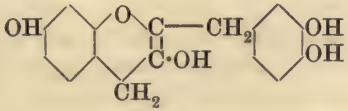


Brazilin.

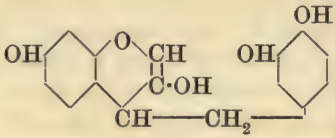


Hæmatoxylin.

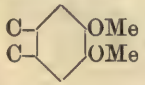
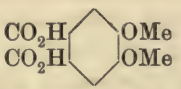
Attention was called to the fact that the formation of large quantities of *m*-hemipinic acid by the oxidation of trimethylbrazilin rendered the formula first proposed by Gilbody and Perkin (I) and that suggested by Feuerstein and Kostanecki (II),*



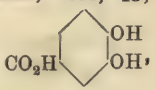
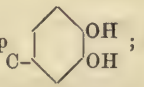
I.



II.

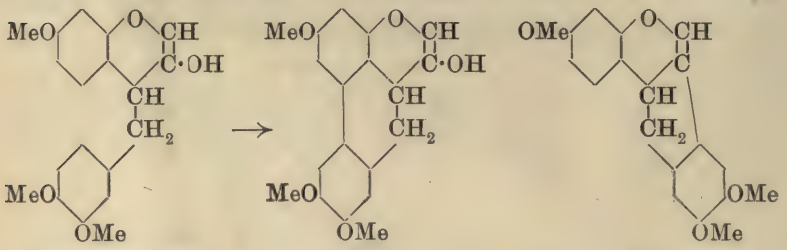
untenable. Neither of these formulæ contains the grouping  and therefore neither can account for the formation of *m*-hemipinic acid,  on oxidation.

Quite recently, Kostanecki and Lampe (*Ber.*, 1902, **35**, 1667) have

* These two formulæ were partly based on Herzig's discovery (*Monatsh.*, 1898, **19**, 738) that brazilin, on fusion with potash, gives protocatechuic acid,  , and that therefore it contains the group  ; it was not until some time afterwards that *m*-hemipinic acid was isolated from the products of the oxidation of trimethylbrazilin.

published a further paper on brazilin in which they state that the discovery of *m*-hemipinic acid among the oxidation products of trimethylbrazilin is not to be considered as evidence against their formula, but rather supports it. Taking their formula as a basis, they assume that either a phenanthrene derivative (III) or an indene derivative (IV) is first formed during the oxidation, and that then the one or the other of these is further oxidised, yielding *m*-hemipinic acid.

So far as can be judged by their paper, the preliminary changes they suppose to take place are represented by the following scheme :



Trimethylbrazilin. III. IV.

Phenanthrene derivative. Indene derivative.

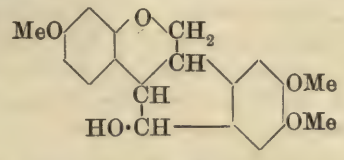
The closing of new rings during the course of an oxidation with permanganate is, to say the least of it, very unusual, and Kostanecki and Lampe do not give examples of known changes of this kind in support of their assumption.

Oxidation by means of alkaline permanganate is generally, and with reason, considered to be one of the most straightforward processes in organic analytical research. Thus, during the great amount of work which has been done on the determination of the constitution of alkaloids—such as papaverine, berberine, hydrastine, and narcotine, for example,—permanganate has been very largely used, and it has always been assumed that the skeleton of the product obtained on oxidation was contained also originally in the substance oxidised.

As trimethylbrazilin, on oxidation, yields *m*-hemipinic acid, and the skeleton of this acid is not to be found in the formula for brazilin suggested by Feuerstein and Kostanecki, the author considers that he was entitled to conclude, as he did, that this formula is incorrect. The explanation of the formation of *m*-hemipinic acid which these chemists are driven to adopt in order to bring the formation of this acid into harmony with their formula is so unusual and unlikely that it can only be entertained if supported by very definite experimental proof, and this is certainly not the case at present.

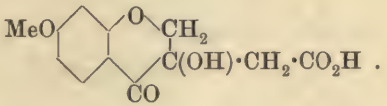
At the end of their recent communication (*Ber.*, 1902, **35**, 1674), Kostanecki and Lampe state " that they have often considered whether

Mr. W. H. Perkin is not after all right in his view that the residue of *m*-hemipinic acid is contained in brazilin," and suggest that, in that case, their formula may be modified to read thus:



This expression is, of course, quite different from their first formula and not merely a modification of it, and in suggesting this new formula they remark in a footnote that they think it strange that Perkin has not discussed its possibility.

As a matter of fact, this formula, to which Herzig has already called attention (*Monatsh.*, 1901, **22**, 2), was carefully considered along with several others not mentioned in the author's publications, but was rejected because it was not in accord with the experimental facts. Kostanecki and Lampe seem to have overlooked the important point that one of the substances formed in the oxidation of trimethylbrazilin is an acid called brazilic acid (this vol., p. 221), the constitution of which has been clearly proved to be



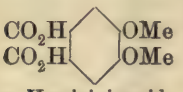
A glance at the formula last suggested by Kostanecki and Lampe and given above, shows at once that this formula does not contain the skeleton of brazilic acid and offers no explanation for the formation of this acid, unless indeed some remarkable molecular change is again assumed to take place during oxidation.

On the other hand, there is no known decomposition of brazilin which cannot be explained by the formula proposed by the author and given at the beginning of this paper, and therefore he is of opinion that, until a more satisfactory expression has been suggested, this formula may well be accepted as best representing brazilin and the second formula, for the same reasons, as that which in the meantime best represents hæmatoxylin.

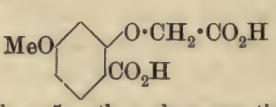
As in the case of all compounds of complicated constitution, synthesis alone can be accepted as conclusive proof of such constitution, and therefore until brazilin or hæmatoxylin has been synthesised, any formula assigned to either of them entirely on the results of analytical work must be considered as being possibly only an approximation to the truth.

During the course of the investigation of brazilin and hæmatoxylin, which has extended over many years, a considerable number of substances have been obtained from both of them, descriptions of some of which have already appeared in brief abstracts published from time to time in the Proceedings. It was the intention of the author to defer the detailed description of the preparation and properties of many of these until conclusive evidence of their nature had been obtained. Since, however, in their recent papers (*loc. cit.*) Kostanecki and his co-workers have commenced the investigation of some of the decomposition products discovered by the author of this paper, it has become necessary to describe in more detail the results, which so far have only appeared in abstract.

The experimental work, which has been described in the three parts of this research already published (*loc. cit.*), has proved that when trimethylbrazilin is oxidised with permanganate at the ordinary temperature, three principal substances are formed, the constitutions of all of which are known; these are

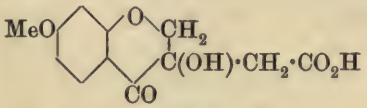


m-Hemipinic acid.



2-Carboxy-5-methoxyphenoxyacetic acid.

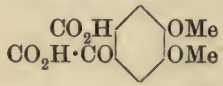
and



Brazilic acid.

The mother liquors from which these acids had separated were found to contain, besides oxalic, acetic, and formic acids and other substances of simple composition, four new and important acids.

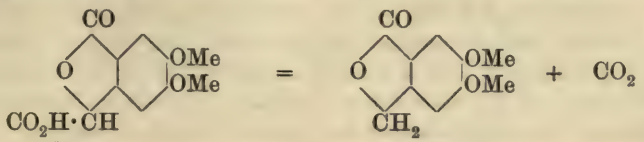
(i) The first of these crystallises in thick prisms of the formula $C_{11}H_{10}O_7,2H_2O$, and becomes anhydrous at 100°; its investigation has proved conclusively that it is the hitherto unknown dimethoxycarboxybenzoylformic acid of the formula



and in proof of this the following points may be mentioned.

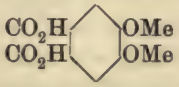
It is a dibasic acid and yields a silver salt of the formula $C_{11}H_8O_7Ag_2$; it combines with hydroxylamine and with semicarbazide and therefore contains the ketonic group. That it is a ketonic acid is further confirmed by its behaviour on reduction, when it readily takes up two atoms of hydrogen and is converted into the corresponding hydroxy-acid, which at once loses water with formation of the lactone.

This *lactone* of *dimethoxycarboxymandelic acid*, when heated above its melting point, loses carbon dioxide with formation of m-*meconine*:



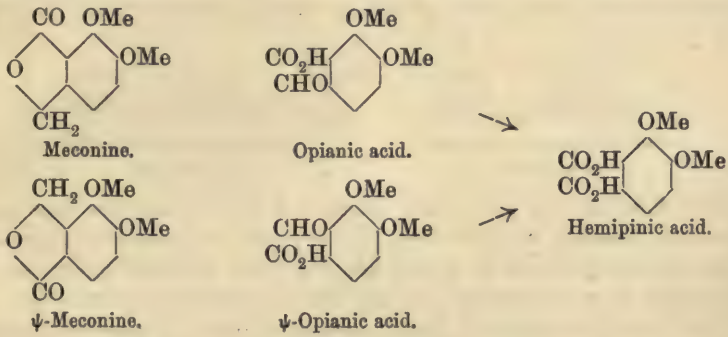
Lactone. *m*-Meconine.

the constitution of which is proved by the fact that, on oxidation, it is converted quantitatively into *m*-hemipinic acid:

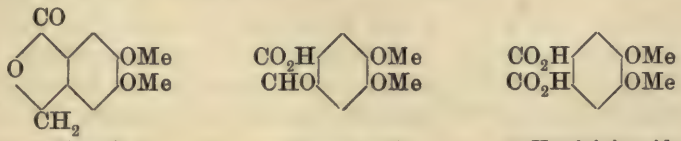


The preparation of *m*-meconine is a matter of considerable interest on account of its relationship to meconine and ψ-meconine, both of which have already been obtained as products of the degradation of narcotine and berberine respectively.

Meconine and ψ-meconine correspond to the two opianic acids and to hemipinic acid,



whereas in the case of *m*-hemipinic acid there can only be one *m*-meconine and *m*-opianic acid;



m-Meconine. *m*-Opianic acid. *m*-Hemipinic acid.

m-Opianic acid is unknown, and, in order to complete the series, a number of experiments were made with the object of preparing this acid, but unfortunately without success. This acid should be formed

by the elimination of carbon dioxide from dimethoxycarboxybenzoylformic acid,

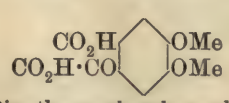
$$CO_2H\cdot CO\cdot C_6H_2(OMe)_2\cdot CO_2H = CHO\cdot C_6H_2(OMe)_2\cdot CO_2H + CO_2,$$

but although carbon dioxide is evolved when this acid is heated, the resulting *m*-opianic acid undergoes condensation with formation of a substance, $C_{20}H_{16}O_8$, described on p. 1025. It is curious that a quantity of *m*-hemipinic acid is formed during this decomposition.

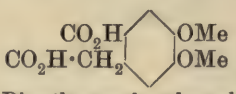
Experiments were also made on the oxidation of *m*-meconine under exactly those conditions which lead from meconine to opianic acid, but in this case also no trace of *m*-opianic acid could be obtained.

(ii) The second new acid which has been obtained from the oxidation of trimethylbrazilin with permanganate is a very sparingly soluble substance of the formula $C_{11}H_{12}O_6$, and melts at about 214°; it is dibasic and is derived from the catechol nucleus of brazilin, since it contains two methoxy-groups and when fused with potash yields a substance the aqueous solution of which gives with ferric chloride an intense green coloration.

Judging from these properties and the fact that it is obtained along with dimethoxycarboxybenzoylformic acid, there can scarcely be a doubt that it is *dimethoxycarboxybenzylformic acid*, the relationship between these two acids being readily seen by writing their formulæ side by side:



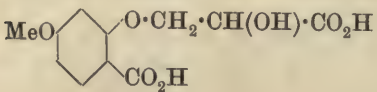
Dimethoxycarboxybenzoylformic acid.



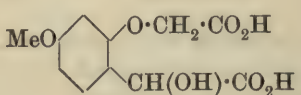
Dimethoxycarboxybenzylformic acid.

(iii) Another new acid, which not only melts at about the same temperature—namely, at 216°—but like the acid just mentioned is also very sparingly soluble in water, has also been isolated in very small quantities from the products of the oxidation of trimethylbrazilin.

This acid is also dibasic, but it is derived from the *resorcyl* nucleus of brazilin, since, on fusion with potash, it yields a substance which gives a violet coloration with ferric chloride. The analyses of the silver salt, $C_{11}H_8O_7Ag_2$, and of the acid itself show clearly that it has the formula $C_{11}H_{10}O_7$, and this fact, taken in conjunction with the simultaneous formation of 2-carboxy-5-methoxyphenoxyacetic acid, $MeO\cdot C_6H_3(CO_2H)\cdot O\cdot CH_2\cdot CO_2H$, and brazilic acid (see next page), make it probable that the constitution of this new acid is represented by one of the two formulæ

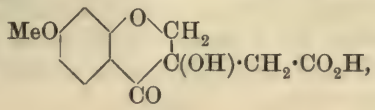


I.



II.

Formula I is to be preferred on account of its close relationship to that of brazilic acid,

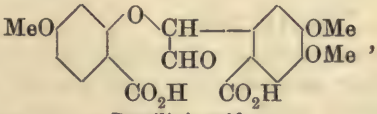


and in the meantime, therefore, this acid will be named *methoxycarboxyphenoxylactic acid.*

(iv) The next acid which has to be discussed is brazilinic acid, an acid which has already been mentioned in a previous paper (Trans., 1901, **79**, 1010) and is formed in considerable quantities when trimethylbrazilin is oxidised with permanganate.

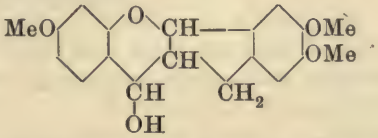
This acid has the formula $C_{19}H_{18}O_9$ and therefore contains the same number of carbon atoms as the trimethylbrazilin, $C_{19}H_{20}O_5$, from which it was derived, and for this reason it was most important that every effort should be made to determine its constitution.

As the result of careful investigation, the author has come to the conclusion that the constitution of this acid is best represented by the formula



Brazilinic acid.

an expression which is derived in a simple manner from the author's formula for trimethylbrazilin,



The evidence on which the above formula for brazilinic acid is based may be briefly summarised as follows:

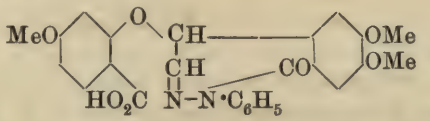
I. It is a dibasic acid, as is shown from the analyses of its *potassium* salt, $C_{17}H_{16}O_5(CO_2K)_2$, *silver* salt, $C_{17}H_{16}O_5(CO_2Ag)_2$, and of its crystalline *methyl ester*, $C_{17}H_{16}O_5(CO_2Me)_2$.

II. The presence of the aldehyde group is shown by the fact that the acid combines with phenylhydrazine and *p*-bromophenylhydrazine in acetic acid solution yielding colourless crystalline condensation products. The compound with phenylhydrazine is formed according to the equation

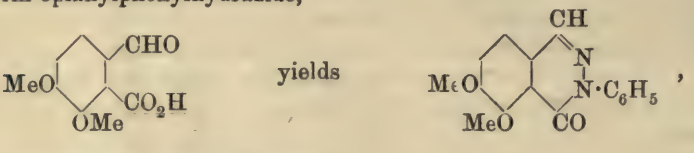
$$C_{19}H_{18}O_9 + C_6H_5{\cdot}NH{\cdot}NH_2 = C_{25}H_{22}O_7N_2 + 2H_2O,$$

and is a monobasic acid, that is to say the phenylhydrazine has

not only reacted with the aldehyde group, but also with one of the carboxyl groups, either from the resorcyl or the catechol nucleus. Which of these carboxyl groups takes part in the reaction it is impossible to say at present, but assuming that it is the catechol carboxyl group, the constitution of the condensation product of brazilinic acid with phenylhydrazine will be



The condensation with *p*-bromophenylhydrazine proceeds on the same lines, and thus the behaviour of brazilinic acid towards these reagents is similar to that of opianic acid, which reacts with phenylhydrazine to form opianylphenylhydrazide,



Liebermann (*Ber.*, 1886, 19, 766)

III. A curious characteristic of brazilinic acid is that, under certain conditions not clearly understood, it is obtained in the form of a stable *hydrate*, $C_{19}H_{18}O_9,H_2O$, which may be dried at 100° without losing water. It melts at 130° with effervescence, solidifies again, and then shows the melting point of brazilinic acid (208°); it is also converted into brazilinic acid when boiled with dilute sulphuric acid. There can be no doubt that in this hydrate the aldehyde group in the acid has been converted into the dihydroxy-group, $\cdot CH(OH)_2$, a change similar to that which takes place when chloral becomes converted into chloral hydrate, $CCl_3\cdot CH(OH)_2$.

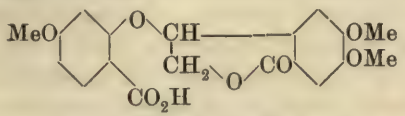
IV. When oxidised by means of permanganate, brazilinic acid yields *m*-hemipinic acid (p. 1033), a decomposition which is readily understood with the aid of the above formula for the former acid. It has not so far been found possible to isolate the acid formed from brazilinic acid by the simple oxidation of the CHO group.

V. Brazilinic acid is very readily reduced by sodium amalgam and is then quantitatively converted into the corresponding dihydro-acid, which, however, at once loses water with formation of the *lactone* of *dihydrobrazilinic acid* (m. p. 228°):

$C_{19}H_{18}O_9$	$\longrightarrow$	$C_{19}H_{20}O_9$	$\longrightarrow$	$C_{19}H_{18}O_8$
Brazilinic acid.		Dihydrobrazilinic acid.		Lactone of dihydrobrazilinic acid.

The constitution of this monobasic lactonic acid (assuming that it is

the catechol carboxyl group which takes place in the formation of the lactone) may be represented thus:

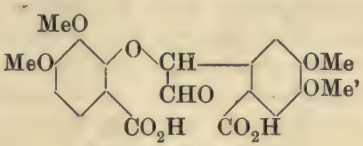


Lactone of dihydrobrazilinic acid.

and the formation of this lactonic acid is strong evidence in favour of the formula of brazilinic acid suggested above.

There are many other interesting reactions of this acid, which are described in detail in the experimental part of this paper but need not be mentioned here. It should, however, be remarked that tetramethylhæmatoxylin, on oxidation with permanganate, yields an acid called hæmatoxylinic acid, a description of which has already appeared in a previous paper (this vol., 239, 243).

The formula there assigned to this acid was

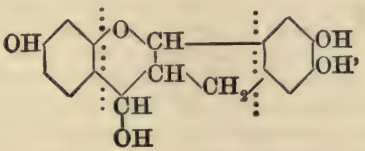


Hæmatoxylinic acid.

and in all its properties it shows an exactly similar behaviour to brazilinic acid.

The Oxidation of Trimethylbrazilin by means of Chromic Acid.

The more important of the very interesting substances which are formed in this oxidation and in the subsequent further treatment of the primary product of the reaction (*trimethylbrazilone*) have been very carefully investigated. And yet, although the changes which are involved in their formation are entirely confined to that section of the author's formula for brazilin which is situated between the dotted lines,



it has not so far been found possible conclusively to demonstrate the nature of these changes.

So far as the determination of the constitution of brazilin is concerned, it may be said that the study of the oxidation of trimethyl

brazilin with chromic acid has not yielded results of such direct fundamental importance as was the case in the oxidation with permanganate. Doubtless, however, as soon as the constitution of the principal products of the oxidation with chromic acid has been clearly proved, this part of the investigation will constitute a valuable confirmation of the results obtained in the permanganate oxidation.

As Gilbody and Perkin first showed (Proc., 1899, **15**, 27), trimethylbrazilin is remarkably easily oxidised by chromic acid, being converted at the ordinary temperature into a substance of the formula $C_{19}H_{18}O_6$, which melts at about 185°* and has been named *trimethylbrazilone*. In the formation of this substance, trimethylbrazilin has therefore taken up one atom of oxygen and lost two atoms of hydrogen, thus:

$$C_{16}H_{10}O(OMe)_3{\cdot}OH + 2O = C_{16}H_8O_2(OMe)_3{\cdot}OH + H_2O.$$

When heated at about 190°, trimethylbrazilone readily loses one mol. of water, forming *anhydrotrimethylbrazilone*, $C_{16}H_{16}O(OMe)_3{\cdot}OH$, a crystalline substance which melts at 198° and still contains a hydroxy-group, since, when digested with acetic anhydride, it yields *acetylanhydrotrimethylbrazilone*,† $C_{16}H_6O(OMe)_3{\cdot}O{\cdot}C_2H_3O$.

This acetyl compound melts at 175° and is identical with the substance which Herzig (*Monatsh.*, 1895, **16**, 913) first obtained by the

* In the abstract of this paper which appeared in the Proceedings (*loc. cit.*), the melting point of trimethylbrazilone was stated to be 191°.

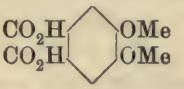
Trimethylbrazilone is a substance which decomposes on heating, and like all substances of this kind it is very difficult to assign a definite melting point to it. The melting point, 191°, originally given by Gilbody and Perkin, which has been the cause of a good deal of confusion, was repeatedly obtained, with very pure material, by plunging the capillary tube into the bath of sulphuric acid heated, in different experiments, between 180° and 191°.

When the determination was done in the ordinary way and the temperature raised somewhat rapidly, the melting point of the substance was always found to be about 183—185°, and this value is therefore adopted in this paper. Repeated recrystallisation of the substance lowers the melting point in a remarkable way, probably owing to the formation of small quantities of anhydrotrimethylbrazilone, and this must be the reason why Herzig (*Monatsh.*, 1902, **23**, 172) gives the melting point at 160°, and Kostanecki and Lampe (*Ber.*, 1902, **35**, 1670) at 165°.

The examination of the decomposition products of trimethylbrazilone prepared with specimens made by different methods has proved conclusively to the author that there is only one substance of this composition formed by the oxidation of trimethylbrazilin with chromic acid even when the conditions are varied through a wide range of temperature and concentration (compare Kostanecki and Lampe, *loc. cit.*, p. 1671). The name β-trimethylbrazilone, which Herzig suggested for his substance of melting point 160°, is therefore no longer necessary.

† The name acetylanhydrotrimethylbrazilone used in this paper applies also to Herzig's trimethylmonoacetyldehydrobrazilin (*Monatsh.*, 1895, **16**, 914), and this alteration in nomenclature was made because the latter name does not indicate the relationship of this acetyl compound to trimethylbrazilone so well as the former does.

oxidation of acetyltrimethylbrazilin. This same acetyl compound is produced at once when trimethylbrazilone is digested with acetic anhydride and sodium acetate, acetylation and elimination of water taking place simultaneously. Anhydrotrimethylbrazilone is characterised by possessing feebly acid properties, since it dissolves in caustic potash and yields a crystalline potassium salt of the formula $C_{16}H_6O(OMe)_3 \cdot OK$; this salt is, however, partially decomposed by water and very readily by carbon dioxide. Herzig (*Monatsh.*, 1902, **23**, 174), who also investigated the action of potash on trimethylbrazilone, has shown that this substance when titrated with hot caustic potash takes up exactly 1 mol. KOH with formation of a solution which, on acidifying, yields anhydrotrimethylbrazilone; there can therefore be no doubt that the salt so formed in solution was the salt of the latter substance and not that of trimethylbrazilone itself. This is confirmed by the fact mentioned in the following paper (this vol., p. 1043) that trimethylbrazilone, when heated with alcoholic potash, is completely converted into anhydrotrimethylbrazilone. The latter substance behaves like an unsaturated compound and is readily oxidised by permanganate, yielding *m*-hemipinic acid and dimethoxycarboxybenzoylformic acid:



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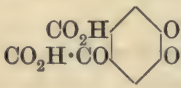


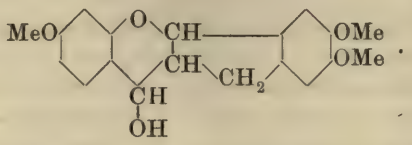
One of the most remarkable properties of trimethylbrazilone is its behaviour towards phenylhydrazine, with which it readily reacts to form a compound of the formula $C_{19}H_{18}O_4$. In the formation of this substance, which melts at 173° and has been called *deoxytrimethylbrazilone*, the phenylhydrazine simply plays the part of a deoxidising agent thus:

$$C_{16}H_7O(OH)_2(OMe)_3 - 2O = C_{16}H_9O(OMe)_3,$$

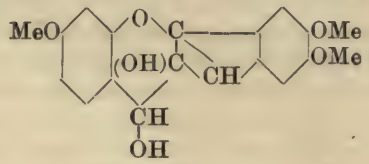
a very unusual property of this reagent.

Deoxytrimethylbrazilone crystallises unchanged from acetic anhydride and therefore does not contain a hydroxy-group; it is unsaturated and very readily attacked by permanganate, but unfortunately no substances of importance could be isolated as the result of this oxidation.

With regard to the question of the constitutions of trimethylbrazilone, dehydrotrimethylbrazilone, and deoxytrimethylbrazilone, it is, at present, not possible to give formulæ to these substances which can be considered as definitely proved, but the author is of the opinion that constitutional formulæ, which are in complete harmony with the properties of these substances, may be easily deduced from his formula for trimethylbrazilin:

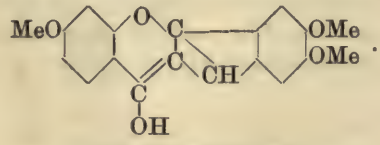


Trimethylbrazilone is formed from trimethylbrazilin by the removal of two atoms of hydrogen and the addition of one atom of oxygen, and its constitution may therefore well be represented thus:



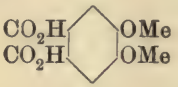
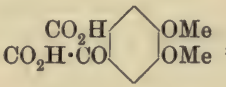
Trimethylbrazilone.

This represents trimethylbrazilone as a saturated dihydroxy-compound, and the removal of two atoms of hydrogen to form a bridged-ring is not without analogy, having often been observed in the terpene series and in other cases. That trimethylbrazilone is a dihydroxy-compound is indicated by the fact that it readily loses water with formation of *anhydrotrimethylbrazilone*. The latter substance still contains one hydroxy-group, since it yields an acetyl compound with acetic anhydride; its constitution, derived from that of trimethylbrazilone, may therefore be represented as



Anhydrotrimethylbrazilone.

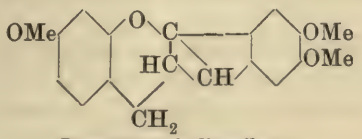
This formula affords a ready explanation of the formation of *m*-hemipinic acid and dimethoxycarboxybenzoylformic acid:

 and  ,

by the oxidation with permanganate.

Deoxytrimethylbrazilone is produced by the removal of two atoms of oxygen from trimethylbrazilone, and these two atoms of oxygen are derived from the two hydroxy-groups, as is clearly proved by the fact that deoxytrimethylbrazilone is incapable of forming an acetyl compound, and therefore does not contain a hydroxy-

group; the formula of this substance may therefore be represented thus:



Deoxytrimethylbrazilone.

Although, then, it is possible with the aid of the author's formula for trimethylbrazilin to deduce formulæ for trimethylbrazilone, anhydrotrimethylbrazilone, and deoxytrimethylbrazilone which are in accordance with the facts, so far as they are at present known, the author does not, of course, intend to suggest that these formulæ are in any way final. Much further experimental evidence is necessary before the constitution of these compounds can be definitely established.

Perhaps the most remarkable reaction which trimethylbrazilone shows is its behaviour with nitric acid, in which it dissolves, forming a pale yellow, crystalline nitro-compound, $C_{19}H_{19}O_9N$, melting at 230°. This process, which takes place almost quantitatively, is not a simple case of nitration, since, in the formation of the new nitro-compound, no water is eliminated, the reaction being one of addition, thus:

$$C_{19}H_{18}O_6 + HNO_3 = C_{19}H_{19}O_9N.$$

From this it follows that, besides nitration, the elements of water must have been taken up in some way, and for this reason the new nitro-compound has been called *nitrohydroxydihydrotrimethylbrazilone*.*

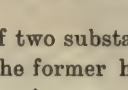
The nitro-compound contains one hydroxy-group, because when boiled with acetic anhydride it yields *nitroacetoxydihydrotrimethylbrazilone*, $NO_2 \cdot C_{16}H_9O_8(O \cdot C_2H_3O)(OMe)_3$, the acetic anhydride showing no tendency to cause the removal of water as it does in the case of the formation of acetylanhydrotrimethylbrazilone from trimethylbrazilone.

The nitro-compound is insoluble in sodium carbonate and is therefore not an acid; it dissolves, however, readily in caustic potash, yielding

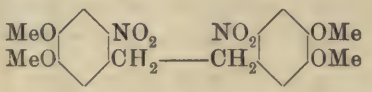
* This substance was first prepared by Gilbody and Perkin in 1899 (Proc., **15**, 27). It was stated at that time that it dissolves in alkalis, yielding an intense purple solution, and on warming that decomposition sets in with the production of *p*-methoxysalicylic acid and two neutral substances which melt at 118° and 206° respectively. Since the nitro-compound did not give the usual qualitative test for nitrogen, it was at first thought that it did not contain this element; subsequent quantitative experiments, however, demonstrated the presence of nitrogen. This same nitro-compound has quite recently been prepared by Bollina, Kostanecki, and Tambor (*Ber.*, 1902, **35**, 1676), who also confirm the above statement as to its behaviour with alkalis.

a most intense violet solution which, on standing, gradually loses this colour, becomes brown, and deposits an amorphous, drab-coloured precipitate.

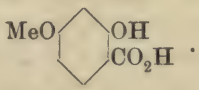
The precipitate consists of two substances melting at 118° and 205° respectively, and of these the former has the composition $C_9H_{11}O_4N$. Since it contains, besides the nitro-group, two methoxy-groups, it must have the formula $NO_2 \cdot C_6H_2Me(OMe)_2$, and there can be no doubt that this substance is identical with the *nitrodimethylhomocatechol* (m.p. 117°),



which H. Cousin (*Ann. Chim. Phys.*, 1898, [vii], **13**, 480), first prepared by the direct nitration and subsequent methylation of homocatechol. The substance of melting point 205° gives numbers closely agreeing with those required for the formula $(C_9H_{10}O_4N)_2$, and it is therefore possibly derived from two molecules of nitrodimethylhomocatechol by the removal of two atoms of hydrogen; that is to say, its constitution is possibly



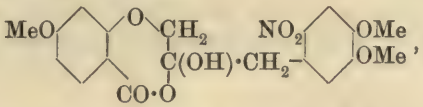
The brown alkaline filtrate from these two substances contains, besides tarry matters, large quantities of *p*-methoxysalicylic acid,



Phenylhydrazine very readily reacts with nitrohydroxydihydrotrimethylbrazilone even at the ordinary temperature and in acetic acid solution yielding a yellowish-red crystalline, substance of the probable formula $C_{24}H_{25}O_4N_5$, together with small quantities of *p*-methoxysalicylic acid, the latter being apparently formed in a secondary reaction. This decomposition was so remarkable and the composition of the resulting product so complex that the reaction was repeated with *p*-bromophenylhydrazine, but with the same result, except, of course, that the nitrogen compound contained bromine and had the formula $C_{24}H_{23}O_4N_5Br_2$.

The author is engaged in the further investigation of this product of the action of phenylhydrazine on the nitro-compound and prefers, for the present, not to speculate as to its constitution. It is, in the first place, difficult to be quite certain of the number of carbon and hydrogen atoms in a substance of such complicated composition, and, secondly, it has not yet been found possible to remove the phenyl-

hydrazine residues and isolate and examine the parent substance. It has, however, been impossible to overlook the great similarity of its properties and those of *nitro-opianylphenylhydrazide* first described by Liebermann (*Ber.*, 1886, **16**, 765), which the author again prepared for direct comparison, and it seems likely that the substance described above belongs to this class. In a recent number of the Proceedings, the author suggested that the formula



or some formula closely allied to it, may possibly represent nitrohydroxydihydrotrimethylbrazilone, and he wishes to reserve the discussion of this formula until the further experiments, on which he is at present engaged, are completed.

Experimental.

Dimethoxycarboxybenzoylformic Acid, $CO_2H{\cdot}CO{\cdot}C_6H_2(OMe)_2{\cdot}CO_2H$.

The details of the method employed in oxidising trimethylbrazilin with permanganate are given in Part I of this research (Trans., 1901, **79**, 1404), and an ethereal extract is there described (p. 1405), from which, on standing, practically the whole of the *m*-hemipinic acid and 2-carboxy-5-methoxyphenoxyacetic acid had crystallised out.

The ethereal mother liquors of these acids, collected from a great number of operations, were evaporated, when a brown oil was deposited, which, on standing, became semi-solid. The whole was dissolved in water, made alkaline with ammonia, calcium chloride added, and heated on the water-bath, when a large quantity of a sparingly soluble calcium salt separated. This was collected on the pump, washed with water, and dissolved in a small quantity of concentrated hydrochloric acid, when, on standing overnight, the whole went nearly solid owing to the separation of a sandy, crystalline precipitate. After collecting on the pump and washing with a little hydrochloric acid, the mass was almost free from inorganic matter and weighed 30 grams (from about 3 kilos. of trimethylbrazilin). On crystallising the substance from water, it was readily separated into a very sparingly soluble acid melting at 214° (see p. 1028), and into readily soluble hard, brownish prisms. The latter, which were first examined, were left on a porous plate exposed to the air until dry. These crystals melt in the water-oven to a gummy mass which gradually becomes hard again, and if the melting point is now taken it is found to be 150°.

As stated in the introduction, this acid has, after careful investigation, been shown to be dimethoxycarboxybenzoylformic acid.

The analysis of the air-dried crystals gave the following results:

0·1505 gave 0·2511 CO_2 and 0·0651 H_2O. C = 45·6; H = 4·8.
0·1649 „ 0·274 CO_2 „ 0·0715 H_2O. C = 45·7; H = 4·8.
$C_{11}H_{10}O_7,2H_2O$ requires C = 45·5; H = 4·8 per cent.

A weighed quantity of the same specimen was heated at 100°, when it did not become constant in weight until after about 10 hours:

0·4021 lost 0·0479 H_2O. H_2O = 11·9.
$C_{11}H_{10}O_7,2H_2O$ requires H_2O = 12·3 per cent.

On standing in the air, the hydrated crystals very slowly give up some of their water, as is shown by the fact that, after 3 weeks, the loss at 100° was only 10·9 per cent. The substance, dried at 100°, gave, on analysis, the following results:

0·1516 gave 0·2836 CO_2 and 0·0591 H_2O. C = 51·0; H = 4·3.
0·1364 „ 0·2567 CO_2 „ 0·0504 H_2O. C = 51·3; H = 4·1.
$C_{11}H_{10}O_7$ requires C = 52·0; H = 3·9 per cent.

Dimethoxycarboxybenzoylformic acid crystallises, therefore, with 2 mols. of water, both of which are driven off at 100°.

Since, however, one of the mols. of water is very much more easily driven off than the other, it is probable that $1H_2O$ is chemically bound, as expressed by the formula $CO_2H{\cdot}C(OH)_2{\cdot}C_6H_2(OMe)_2{\cdot}CO_2H$. As is well known, glyoxylic acid itself shows a similar behaviour. When dimethoxycarboxybenzoylformic acid is mixed with concentrated sulphuric acid, it dissolves, forming a yellow solution which, on standing, becomes an intense brownish-orange; on heating this solution on the water-bath, a gas (probably carbon monoxide) is given off and the solution becomes nearly colourless.

If the finely powdered acid is mixed with benzene and a trace of thiophen and then shaken with half its volume of sulphuric acid, the latter first becomes reddish-brown, the benzene acquiring a sage-green colour. After a time, the sulphuric acid becomes intense olive-green, and on cautiously diluting with water, the colour becomes a brighter green, then a dark green powder is precipitated, which, on the addition of acetone, dissolves, forming a bright malachite-green solution. This reaction is similar to that shown by phenylglyoxylic acid (Claisen, *Ber.*, 1879, **12**, 1505).

Salts of Dimethoxycarboxybenzoylformic Acid.—In order to determine the basicity of the acid, 0·3513 gram of the anhydrous acid was dissolved in water and titrated with decinormal soda, when it required

for neutralisation 0·1096 gram NaOH; an acid, $C_{11}H_{10}O_7$, if dibasic, should have neutralised 0·1107 gram NaOH.

The *silver* salt, $C_{11}H_8O_7Ag_2$, was obtained, on adding silver nitrate to a slightly alkaline solution of the ammonium salt, as a fine powder, like barium sulphate in appearance, and, like this, it readily passes through the paper. It is very sparingly soluble in, and does not decompose on boiling with, water. On analysis:

0·2448 gave 0·2522 CO_2, 0·0422 H_2O, and 0·1132 Ag. C = 28·1; H = 1·9; Ag = 46·2.

$C_{11}H_8O_7Ag_2$ requires C = 28·2; H = 1·7; Ag = 46·2 per cent.

This analysis shows that the silver salt is derived from an acid of the formula $CO_2H{\cdot}CO{\cdot}C_6H_2(OMe)_2{\cdot}CO_2H$, and not from the hydrated formula given above. A neutral solution of the ammonium salt of the acid behaves with reagents as follows.

Calcium chloride gives no precipitate in the cold, but on boiling a sparingly soluble crystalline calcium salt separates at once. *Barium chloride* gives a white, gelatinous precipitate in the cold. *Copper sulphate* does not give a precipitate.

Action of Hydroxylamine on the Acid.—Very curious results were obtained on attempting to prepare the oxime of the acid. Two grams of the acid were dissolved in water, mixed with a solution of 4 grams of caustic potash, and then 2 grams of hydroxylamine hydrochloride added and the whole allowed to stand overnight. On acidifying, nothing separated, and it was found necessary to shake at least twenty times with fresh quantities of ether in order to extract the product. The ethereal solution was dried over calcium chloride and evaporated to a small bulk, when a crystalline precipitate separated which was very sparingly soluble in ether and, under the microscope, was seen to consist of warty masses. On analysis:

0·1576 gave 0·2958 CO_2 and 0·0650 H_2O. C = 51·2; H = 4·5.
0·1860 „ 5·3 c.c. nitrogen at 20·5° and 751 mm. N = 3·2.

The normal oxime would have the formula $C_{11}H_{11}O_7N$, which requires C = 49·1, H = 4·1, N = 5·2 per cent., and it is evident that the numbers obtained do not at all agree with those required for this formula.

The substance was now dissolved in excess of potash and treated with a large excess of hydroxylamine; it was again extracted as before and twice recrystallised from ether. A nitrogen determination was made:

0·1118 gave 3 c.c. nitrogen at 16° and 753 mm. N = 3·1.

It was then found that the substance crystallised beautifully from water in slender needles, which shrink together at about 178° without

melting and then decompose, with evolution of gas, between 210° and 220°. After twice crystallising the substance from water, the following results were obtained on analysis:

0·1527 gave 0·2899 CO_2 and 0·0684 H_2O. C = 51·8; H = 4·9.
0·2500 „ 6·8 c.c. nitrogen at 17·4° and 765 mm. N = 3·1.

These results agree fairly closely with those first obtained, and it is difficult to understand what this well-characterised substance can be. A molecular compound of the oxime and the unchanged acid $C_{11}H_{11}O_7N, C_{11}H_{10}O_7$ requires C = 52·2; H = 3·7; N = 2·8 per cent.

When a solution of the acid in water is mixed with excess of semicarbazide acetate, a crystalline substance soon begins to separate in balls of needles; these become soft at 255° and decompose at 262—265°, but the amount of substance was not sufficient for further investigation.

Action of Heat on Dimethoxycarboxybenzoylformic Acid.

Formation of Metahemipinic Acid, $(CO_2H)_2C_6H_2(OMe)_2$.—When about 0·2 gram of the acid is heated in a test-tube in a metal bath at 200—205°, a gas partly consisting of carbon dioxide is evolved, and as soon as the evolution has ceased, the residue, on cooling, sets to a brown resin which, when boiled with water, becomes crystalline but does not dissolve. The precipitate was collected, dissolved in boiling methyl alcoholic potash, the solution evaporated until free from methyl alcohol, and acidified, when a small quantity of a crystalline substance separated which crystallised from dilute acetic acid in needles and melted at 212° with decomposition.

This acid is probably *m*-opianic acid, $CHO{\cdot}C_6H_2(OMe)_2{\cdot}CO_2H$, but, unfortunately, the yield was so small that it was not possible to analyse or examine it any further. In the hope that the decomposition would proceed more satisfactorily in aqueous solution, the remainder of the acid (2 grams) was dissolved in 20 c.c. of water and heated in a sealed tube at 200° for 1 hour. The very voluminous mass of needles which separated on cooling was collected, the mother liquor again heated at 200°, when a further quantity of crystals was obtained, and this operation was continued until no more crystals were formed.

The combined crops of crystals were then crystallised from acetic acid, from which the new substance separated in needles melting above 260°. On analysis:

0·1235 gave 0·2828 CO_2 and 0·0513 H_2O. C = 62·5; H = 4·6.
$C_{20}H_{16}O_8$ requires C = 62·5; H = 4·2 per cent.

This substance is practically insoluble in water, but dissolves in sodium carbonate, and, on acidifying, separates as a curious, gelatinous

mass which is insoluble in water and remains gelatinous even after boiling.

Titration with decinormal caustic soda yielded results which point to the acid being a monobasic lactone acid of the formula $C_{20}H_{16}O_8$. Thus 0·1488 gram of the acid required 0·0162 gram NaOH for neutralisation, whereas this quantity of a monobasic acid, $C_{20}H_{16}O_8$, requires 0·0155 gram NaOH.

On adding excess of soda, boiling, and then titrating back with acid, it was found that 0·0328 gram NaOH had been neutralised; this points to the acid having become dibasic, in which case the amount neutralised should have been 0·0318 gram NaOH. This acid is very probably formed from 2 mols. of *m*-opianic acid by the elimination of 2 mols. of water, thus:

$$2CHO\cdot C_6H_2(OMe)_2\cdot CO_2H = C_{20}H_{16}O_8 + 2H_2O,$$

but in what way this condensation takes place there is no evidence to show.

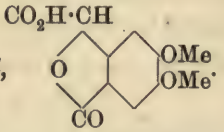
The aqueous mother liquors from this very sparingly soluble condensation product were repeatedly extracted with ether, when the ethereal solution, after drying over calcium chloride and evaporating to a small bulk, deposited on standing a crystalline crust which melted at 188° and consisted of nearly pure *m*-hemipinic acid:

0·1283 gave 0·252 CO_2 and 0·0517 H_2O. C = 53·1; H = 4·4.

$C_{10}H_{10}O_6$ requires C = 53·5; H = 4·4 per cent.

The amount of *m*-hemipinic acid obtained in this way was considerably more than that of the condensation product described above.

Lactone of Dimethoxycarboxymandelic Acid,



This lactonic acid is produced by the reduction of dimethoxycarboxybenzoylformic acid with sodium amalgam.

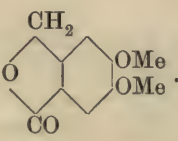
The acid was dissolved in water, neutralised with sodium carbonate, and the solution reduced in the ordinary way with a large excess of sodium amalgam, added in small quantities at a time. As the reduction product was not precipitated on acidifying, the whole was saturated with ammonium sulphate and extracted 20 times with ether, the ethereal solution, after drying over calcium chloride, was then evaporated to a small bulk when, on standing, a colourless, crystalline acid separated. The crystals were collected on the pump, washed with ether, and analysed;

0·1597 gave 0·3245 CO_2 and 0·0616 H_2O. C = 55·4; H = 4·3.
$C_{11}H_{10}O_6$ requires C = 55·4; H = 4·2 per cent.

The *lactone* of *dimethoxycarboxymandelic acid* melts at about 207° with decomposition and is very sparingly soluble in dry ether; it dissolves readily in hot water and separates on cooling in stellate groups; when heated a few degrees above its melting point, it decomposes rapidly into carbon dioxide and *m*-meconine (see next section). The lactone showed the following behaviour on titration with decinormal sodium hydroxide. The solution of 0·0949 gram in water required for neutralisation 0·0160 gram NaOH, but when boiled with excess of soda and then titrated back it was found that 0·032 NaOH had been neutralised. The amount taken of a monobasic acid should neutralise 0·015 gram, and on becoming dibasic 0·03 gram NaOH.

This experiment shows therefore that the substance is a monobasic lactonic acid.

m-*Meconine*,



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It has already been mentioned that the lactone of dimethoxycarboxymandelic acid, when heated above its melting point, is decomposed into carbon dioxide and *m*-meconine. In carrying out this decomposition, it is only necessary to heat the lactonic acid at 210—220° until the evolution of carbon dioxide has ceased, and then to dissolve the residue in a little boiling alcohol. The solution, on cooling, deposits needle-shaped crystals, which after recrystallising from the same solvent, are obtained quite colourless and consist of pure *m*-meconine. On analysis:

0·1556 gave 0·3530 CO_2 and 0·0735 H_2O. C = 61·8; H = 5·2.
$C_{10}H_{10}O_7$ requires C = 61·8; H = 5·1 per cent.

m-*Meconine* melts at 155—156° and is almost insoluble in cold water; it dissolves, however, in much boiling water and separates, on cooling, in woolly needles; it is also sparingly soluble in ether, from which it crystallises in prismatic needles.

Cold dilute potash does not dissolve *m*-meconine, but on warming it rapidly passes into solution, evidently in the form of the potassium salt of the corresponding *m*-meconinic acid, $CH_2(OH)\cdot C_6H_2(OMe)_2\cdot CO_2H$. When the solution is cooled well and acidified, needle-shaped crystals soon separate, which at first are soluble in sodium carbonate and therefore consist of the free acid; on standing, but much more rapidly on warming, the crystals become insoluble in dilute alkali, water having been eliminated with re-formation of the lactone. *m*-Meconine

dissolves in hot dilute ammonia, but on evaporation the solution loses ammonia and the lactone is again deposited.

Oxidation of m-*Meconine to* m-*Hemipinic Acid.*—The solution of *m*-meconine in dilute potash is only very slowly attacked by permanganate in the cold, but on warming on the water-bath oxidation takes place fairly readily.

In investigating this oxidation, 0·5 gram of *m*-meconine was dissolved in potash, the solution heated on the water-bath, and permanganate added until the colour remained permanent. After destroying the excess of permanganate by adding sodium sulphite, the whole was filtered, and the filtrate and washings of the manganese precipitate were evaporated to a small bulk. When the alkaline solution was acidified with hydrochloric acid, nothing separated at first, but on standing, a mass of needles crystallised out; these were collected and purified by recrystallisation from water. The needle-shaped crystals thus obtained melted at 194° with decomposition and gave on analysis the following result:

0·1551 gave 0·3033 CO_2 and 0·0603 H_2O. C = 53·3; H = 4·3.
$C_{10}H_{10}O_6$ requires C = 53·1; H = 4·4 per cent.

That this was *m*-hemipinic acid was proved by converting it into the characteristic ethylimide which melted at 230° (compare Trans., 1901, 79, 1406).

The yield of *m*-hemipinic acid obtained by oxidising *m*-meconine with permanganate is probably almost a quantitative one. An experiment on the oxidation of *m*-meconine with manganese dioxide and sulphuric acid was tried in the hope of obtaining the corresponding *m*-opianic acid, but without result, most of the *m*-meconine being recovered unchanged even after long boiling with the oxidising agent. This is rather remarkable, as this method works well in converting ordinary meconine into opianic acid.

Dimethoxycarboxybenzylformic Acid, $CO_2H{\cdot}CH_2{\cdot}C_6H_2(OMe)_2{\cdot}CO_2H$.

This acid is obtained, together with dimethoxycarboxybenzoylformic acid, by the process given on p. 1022, and as it is very sparingly soluble it is readily separated from the latter by crystallisation from water. After twice recrystallising, the colourless, needle-shaped crystals softened at about 205° and melted at 214° with vigorous decomposition. On analysis:

0·1501 gave 0·3021 CO_2 and 0·0689 H_2O. C = 54·9; H = 5·1.
0·1208 „ 0·2419 CO_2 „ 0·0552 H_2O. C = 54·7; H = 5·1.
$C_{11}H_{12}O_6$ requires C = 55·0; H = 5·0 per cent.

Dimethoxycarboxybenzylformic acid is very readily soluble in hot

water and separates almost completely on cooling in silky needles; it dissolves readily in alcohol, and the alcoholic solution gives, on the addition of ferric chloride, a rather intense orange-yellow coloration. That the acid is dibasic was shown by the results obtained on the titration with decinormal caustic soda, when 0·1711 gram required for neutralisation 0·058 gram NaOH, whereas this amount of a dibasic acid, $C_{11}H_{12}O_6$, should neutralise 0·057 gram NaOH.

When fused with potash, the acid gives a clear, almost colourless mass, which, on acidifying and extracting with ether, yields a colourless syrup; this dissolves readily in water and gives with ferric chloride an intense green, turning to violet and then to red on the addition of sodium bicarbonate. This proves that the acid is a derivative of the catechol nucleus of brazilin.

Unfortunately, the amount of this new acid which is formed under the conditions of oxidation employed, is exceedingly small (about 1·3 grams from 3 kilos. of trimethylbrazilin); it has therefore been impossible to investigate its behaviour on oxidation or in many other interesting directions.

Acid of Melting Point 216° (*Resorcyl Derivative*) *from the Oxidation of Trimethylbrazilin with Permanganate; probably Methoxycarboxyphenoxylactic Acid*, $MeO{\cdot}C_6H_3(CO_2H){\cdot}O{\cdot}CH_2{\cdot}CH(OH){\cdot}CO_2H$.

When the mother liquors of the calcium salt of dimethoxycarboxybenzoylformic acid (p. 1022) are evaporated, a further considerable quantity of a calcium salt separates; this was collected, washed with water, and dissolved in dilute hydrochloric acid, when, on cooling, a mass of brownish crystals separated which melted at about 208°, and even after repeated recrystallisation from water with the aid of animal charcoal were still very dark coloured. From acetic acid, however, the substance separated in satiny crystals which, after washing with acetic acid, were almost colourless, and when rapidly heated softened at 208° and melted at 216°. The mother liquors (*b*) from the calcium salt were acidified and extracted repeatedly with ether, the ethereal solution dried over calcium chloride, and evaporated, when a syrupy residue was obtained which, after standing for some weeks, became semi-solid. In contact with porous porcelain, the oily impurity was rapidly absorbed, and the residue, dissolved in a little hot water and neutralised with sodium carbonate, gave, on standing, a mass of crystals of the sodium salt of brazilic acid.

The sodium salt was recrystallised, decomposed with hydrochloric acid, and the brazilic acid recrystallised from water. It melted at 129—130° and gave on analysis:

0·1146 gave 0·2402 CO_2 and 0·0504 H_2O. C = 57·1; H = 4·9.
$C_{12}H_{12}O_6$ requires C = 57·2; H = 4·8 per cent.

The amount of this acid obtained from these mother liquors was rather more than 3 grams from 3 kilos. of trimethylbrazilin.

Examination of the acid melting at 216°.—This acid gave on analysis the following numbers:—

0·1368 gave 0·2606 CO_2 and 0·0514 H_2O. C = 51·9; H = 4·1.
0·1232 „ 0·2345 CO_2 „ 0·0455 H_2O. C = 52·0; H = 4·1.
$C_{11}H_{10}O_7$ requires C = 52·0; H = 3·9 per cent.

It is very sparingly soluble in water but dissolves readily in alcohol or hot glacial acetic acid; it is, however, only sparingly soluble in acetic acid in the cold. The solution in dilute alcohol gives no coloration wth ferric chloride. When heated at 220—225°, the acid decomposes with evolution of carbon dioxide, and a small quantity of a crystalline substance sublimes; the residue which solidifies smells very strongly of coumarin and crystallises from water, but owing to lack of material this interesting substance could not be further investigated. When fused with potash, the acid of melting point 216° yields a slightly brownish product, and on acidifying, extracting with ether, and evaporating off the ether, a syrup is left which, when dissolved in water, gives with ferric chloride an intense violet coloration, showing that the acid is derived from the resorcyl nucleus in brazilin.

That the acid melting at 216° is dibasic was shown first by titration with decinormal caustic soda, when 0·0487 gram required for neutralisation 0·0158 gram NaOH; whereas the amount taken of a dibasic acid, $C_{11}H_{10}O_7$, should neutralise 0·0153 gram NaOH.

In order further to control the formula of the substance, the remainder of the acid was converted into the *silver* salt, $C_{11}H_8O_7Ag_2$, which was obtained as a white, gelatinous precipitate on adding silver nitrate to a slightly alkaline solution of the ammonium salt. On analysis:

0·2312 gave 0·2390 CO_2, 0·0399 H_2O, and 0·1064 Ag. C = 28·2; H = 1·9; Ag = 46·0.
$C_{11}H_8O_7Ag_2$ requires C = 28·2; H = 1·7; Ag = 46·1 per cent.

As explained in the introduction (p. 1014), it is probable that this substance is methoxycarboxyphenoxylactic acid, and is very possibly produced by the oxidation of brazilic acid.

Brazilinic Acid, $(OMe)_3C_{13}H_6O(CO_2H)_2{\cdot}CHO$.

This acid has already been briefly described in Section I of this research (Trans., 1901, 79, 1401), and two analyses were given which clearly

point to the formula $C_{19}H_{18}O_9$. This formula has since been confirmed by the analysis of a number of salts and other derivatives of the acid. Indeed the great importance of this acid, due to the fact that it contains the same number of carbon atoms as the trimethylbrazilin from which it is obtained by oxidation, has led to its being most carefully investigated.

Brazilinic acid melts at 208—210° and is readily soluble in hot alcohol or acetic acid, but only sparingly so in chloroform or benzene and almost insoluble in cold water. It dissolves slightly in boiling water and separates on standing in warty masses; it is most conveniently recrystallised from glacial acetic acid. It dissolves readily in ammonia or sodium carbonate and when precipitated from solutions of its salts, it always separates as a sticky mass, which gradually hardens, especially if kneaded with cold water.

Salts of Brazilinic Acid.—That this acid is dibasic was first shown by titration with decinormal sodium hydroxide, when 0·237 gram required for neutralisation 0·0497 gram NaOH, whereas this amount of a dibasic acid should neutralise 0·0486 gram NaOH.

Potassium Salt, $C_{19}H_{16}O_9K_2$.—This salt is easily prepared by adding a filtered solution of alcoholic potash to a solution of the acid in absolute alcohol. The salt, which rapidly separates in a crystalline form, is collected on the pump, washed with alcohol, and dried at 100°. On analysis:

0·3077 gave 0·1121 K_2SO_4. K = 16·4

$C_{19}H_{16}O_9K_2$ requires K = 16·7 per cent.

This salt is readily soluble in water and is decomposed by hydrochloric acid, but apparently not by acetic acid, yielding a white, oily precipitate which soon becomes sticky and, in contact with water, quite hard; after drying on a porous plate it melted at 208°, the melting point of brazilinic acid.

The *silver* salt, $C_{19}H_{16}O_9Ag_2$, was obtained as a white, amorphous precipitate on adding silver nitrate to a warm, dilute, slightly alkaline solution of the ammonium salt. Two different specimens gave on analysis the following results:

0·2639 gave 0·3576 CO_2, 0·0607 H_2O, and 0·0932 Ag. C = 37·0; H = 2·5; Ag = 35·2

0·2313 gave 0·3139 CO_2, 0·0556 H_2O, and 0·0798 Ag. C = 37·3; H = 2·7; Ag = 35·7.

$C_{19}H_{16}O_9Ag_2$ requires C = 37·7; H = 2·6; Ag = 35·7 per cent.

A slightly alkaline solution of the ammonium salt of brazilinic acid showed the following behaviour with reagents.

Barium chloride gave no precipitate in the cold, but on boiling a spar-

ingly soluble crystalline barium salt; *calcium chloride* or *zinc sulphate*, no precipitate; *copper sulphate*, a pale green, and *lead acetate*, a white, amorphous precipitate.

Methyl Brazilinate, $C_{17}H_{16}O_5(CO_2 \cdot CH_3)_2$.—This ester is very readily prepared by boiling brazilinic acid with methyl alcohol and a little sulphuric acid for two hours and then allowing the product to stand overnight. A considerable quantity of the methyl ester will then have crystallised out and the rest may be precipitated by adding water. The solid is collected, washed with dilute sodium carbonate, and purified by recrystallisation from methyl alcohol, from which it separates in glistening prisms. On analysis:

0·2003 gave 0·4437 CO_2 and 0·0941 H_2O. C = 60·4; H = 5·2.
0·1877 „ 0·4160 CO_2 „ 0·0886 H_2O. C = 60·4; H = 5·3.
$C_{21}H_{22}O_9$ requires C = 60·3; H = 5·3 per cent.

This methyl ester melts at 117° and is readily soluble in hot methyl alcohol, acetic acid, or benzene, but only sparingly so in cold methyl alcohol or light petroleum. It dissolves in sulphuric acid with a yellow colour which, on standing, becomes orange. The same methyl ester is obtained when brazilinic acid is heated in a sealed tube with sodium methoxide and methyl iodide at 150° for two hours.

Behaviour of Brazilinic Acid with Reagents.—Brazilinic acid is a saturated acid, as is shown by the fact that its solution in cold dilute sodium carbonate does not decolorise permanganate except on long standing; prolonged contact with the oxidising agent converts it into hemipinic and oxalic acids, as explained on p. 1033.

Brazilinic acid is coloured an intense orange-red by sulphuric acid and then dissolves, producing an orange-red solution the colour of which remains for some days (compare the behaviour of the lactone of dihydrobrazilic acid under similar circumstances, p. 1039).

Brazilinic acid is very readily acted on by nitric acid and dissolves in the strong acid with an intense red colour. If the finely-powdered acid is heated to boiling with dilute nitric acid (1 part of ordinary concentrated acid to 15 parts of water), it dissolves, forming a pale yellow solution from which a sparingly soluble crystalline substance separates during the boiling. This crystallises from acetic acid in pale yellow prisms which sinter at 230° and melt at 245—247°; it contains nitrogen and is, apparently, a nitro-acid, but it was not further investigated.

Action of Phenylhydrazine and p-*Bromophenylhydrazine.*—When brazilinic acid dissolved in acetic acid, is mixed with an excess of freshly distilled phenylhydrazine, a violet-coloured solution is produced, and this, after standing for some hours, gives a resinous precipitate on adding water. If, after washing with water, this is dissolved in hot

methyl alcohol, the solution, on cooling, deposits a mass of needle-shaped crystals which, after recrystallising from methyl alcohol, melt at 227°.

On analysis:

0·2061 gave 10·5 c.c. nitrogen at 20° and 755 mm. N = 5·8.

$C_{25}H_{24}O_8N_2$ requires N = 5·8; $C_{25}H_{22}O_7N_2$ requires N = 6·0 per cent.

The first of these formulæ is that of the hydrazone of brazilic acid, a substance which would still be a dibasic acid; whereas the second formula is derived from the first by the elimination of water between the NH group of the phenylhydrazine residue and one of the carboxyl groups and would therefore represent a monobasic acid. In order to decide between these two formulæ, the substance was titrated with decinormal sodium hydroxide, when 0·1417 gram required for neutralisation 0·0122 gram NaOH; this shows that the substance is a monobasic acid of the formula $C_{25}H_{22}O_7N_2$, as in this case the amount taken should have neutralised 0·0126 gram NaOH. The product of the action of phenylhydrazine on brazilinic acid is therefore *anhydro-brazilinic acid phenylhydrazone.*

Exactly similar results were obtained in studying the action of *p*-bromophenylhydrazine on brazilinic acid. The substance produced crystallised from methyl alcohol as a felted mass of colourless needles, which melted at 180—182° with slight previous softening, and appeared partially to solidify again when heated at 200—210°. On analysis:

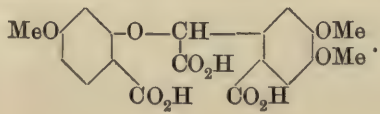
0·1438 gave 6·8 c.c. nitrogen at 17° and 750 mm. N = 5·4.

$C_{25}H_{21}O_7N_2Br$ requires N = 5·2 per cent.

The titration of this substance gave the following results: 0·1311 gram required for neutralisation 0·103 gram NaOH, whereas this amount of a monobasic acid of the formula $C_{25}H_{21}O_7N_2Br$ would neutralise 0·0097 gram NaOH. This substance is therefore *anhydro-brazilinic acid bromophenylhydrazone.*

Oxidation of Brazilinic Acid with Permanganate. Formation of m-*Hemipinic Acid*, $(CO_2H)_2C_6H_2(OMe)_2$.

The oxidation of brazilinic acid was carried out under a great variety of conditions, in the hope that it would be found possible to isolate the tribasic acid of the formula



which would result from the simple oxidation of the aldehyde group, but although there were frequently indications of the formation of an acid of this kind, it could never be isolated in a pure state.

The principal products of the oxidation were always *m*-hemipinic acid and oxalic acid. In one experiment, brazilinic acid was dissolved in dilute sodium carbonate and oxidised with permanganate at about 40° until the colour remained permanent on standing overnight. After removing the excess of permanganate by the addition of sodium sulphite, the filtrate and washings of the manganese precipitate were evaporated, acidified, and extracted repeatedly with ether. The ethereal solution was dried over calcium chloride and evaporated to a small bulk, when, on standing, a crystalline crust separated and after recrystallising from water, hard, colourless crystals were obtained which melted at about 190° and consisted of *m*-hemipinic acid. On analysis:

0·1603 gave 0·3112 CO_2 and 0·0648 H_2O. C = 52·9; H = 4·5.

$C_{10}H_{10}O_6$ requires C = 53·1; H = 4·4 per cent.

The aqueous liquors which had been extracted with ether were evaporated to dryness and the residue extracted with ether in a Soxhlet apparatus, when on distilling off the ether quantities of oxalic acid were obtained together with traces of some other acid which could not be isolated in a pure condition.

Action of Fused Caustic Potash on Brazilinic Acid.

In endeavouring to discover the constitution of this acid, one of the first decompositions investigated was the behaviour of the acid with fused potash. The acid (2 grams) was dissolved in caustic potash solution (containing 30 grams of KOH) and the solution evaporated in a silver crucible and gradually heated to 190—210°, at which temperature it was kept for half an hour. On dissolving the dark brown product in water and acidifying, nothing separated; the product was therefore extracted with ether, when on distilling off the ether a dark brown residue was obtained which was dissolved in much water and precipitated with lead acetate. The lead salt was decomposed with sulphuretted hydrogen in the usual way, when the filtrate from the lead sulphide, on evaporation to a small bulk, deposited yellow, crystalline crusts, which after crystallising from water acidified with acetic acid, to prevent oxidation, melted at about 250° with rapid decomposition. On analysis:

0·1916 gave 0·3917 CO_2 and 0·0670 H_2O. C = 55·7; H = 3·9.

0·211 „ 0·4288 CO_2 „ 0·0715 H_2O. C = 55·4; H = 3·8.

$C_{16}H_{12}O_9$ requires C = 55·2; H = 3·4 per cent.

This substance, which may provisionally be called *norbrazilinic acid*, is sparingly soluble in water and its solution gives, with ferric chloride, an intense catechol reaction. Apparently the action of the potash has been simply to remove the methyl groups in brazilinic acid and to replace them by hydrogen, hence the catechol reaction, but the substance thus formed has, so far, not been further examined.

Action of Alcoholic Potash on Brazilinic Acid.

In studying this decomposition, powdered brazilinic acid (2 grams) is placed in a pressure tube with 20 c.c. of strong alcoholic potash and the tube sealed. It is then warmed in a water-bath and well shaken, when the contents become almost solid owing to the separation of the potassium salt. The tube is now heated at 155° for four hours, either in a rocking arrangement, or if this is not available, the iron box is tilted backwards and forwards from time to time, to ensure a perfect mixing, as, if this is not done, the result is frequently very unsatisfactory.

On opening the tube, there is no pressure and the contents consist of a pale yellow liquid, all the solid having disappeared. The whole is mixed with water, evaporated until free from alcohol, when, if the operation has been successful, there will be no darkening, but if the temperature has been too high, the liquid becomes brown and ultimately black. On acidifying the solution, a sticky precipitate separates; this is collected, boiled with 150 c.c. of water for 5 minutes, well ground up with dilute sodium carbonate (which dissolves about half) and filtered.

The residue dissolves readily in methyl alcohol, and on cooling and stirring vigorously, a quantity of crystals separate; these are collected and recrystallised from the same solvent, when the substance is readily obtained pure in the form of colourless needles which melt at 141—142°. On analysis:

0·1458 gave 0·3597 CO_2 and 0·0841 H_2O. C = 67·3; H = 6·3.
0·1788 „ 0·4402 CO_2 „ 0·1030 H_2O. C = 67·2; H = 6·4.
$C_{17}H_{18}O_5$ requires C = 67·6; H = 5·9 per cent.

This substance, which is apparently derived from brazilinic acid simply by the elimination of 2 mols. of carbon dioxide, is readily soluble in hot methyl alcohol but only sparingly so in the cold; it dissolves readily in warm benzene, but is only sparingly soluble in light petroleum, and almost insoluble in water.

It does not dissolve in sodium carbonate, even on boiling, or in aqueous potash, but dissolves in hot methyl alcoholic potash, and on adding water and boiling away the alcohol, it remains in solution and is not precipitated by passing carbon dioxide; on acidifying with hydrochloric

acid, a white caseous precipitate is obtained. This, on warming with water, becomes crystalline and insoluble in potash; it then melts at 138° and is identical with the original substance. It dissolves in sulphuric acid, yielding an intense orange solution, and is coloured orange-red by hydrobromic or nitric acids and as these reactions are exactly the same as those shown by brazilinic acid under the same conditions, it seems probable that the two substances are similarly constituted, and that the heating with alcoholic potash has not brought about any fundamental change in structure. That the substance of melting point 142° should exhibit the properties of a lactone is very remarkable and requires further investigation. The aqueous sodium carbonate filtrate obtained in the purification of this substance (see above) yields on acidifying an amorphous acid, which after drying on a porous tile resembles powdered chalk; it has not yet been sufficiently investigated.

Action of Bromine and Potash on Brazilinic Acid.

When a strong solution of the potassium salt of brazilinic acid is mixed with a strong solution of potassium hypobromite coloured with bromine, a very sparingly soluble potassium salt gradually separates. This was collected, recrystallised from water, and decomposed by hydrochloric acid, when a colourless, crystalline acid was obtained which crystallised from acetic acid in needles and melted at 170°. On analysis:

0·17 gave 0·20 CO_2 and 0·0384 H_2O. C = 32·1; H = 2·5.

0·2053 gave 0·2241 AgBr. Br = 46·5.

$C_{19}H_{14}O_9Br_4$ requires C = 32·3; H = 2·0; Br = 45·3 per cent.

The *potassium* salt mentioned above gave on analysis the following result:

0·4376 gave 0·0946 K_2SO_4. K = 9·6.

$C_{19}H_{12}O_9Br_4K_2$ requires K = 9·9 per cent.

From these results, it would appear that the substance of melting point 170° is *tetrabromobrazilinic acid*, substitution without oxidation having taken place under the conditions mentioned above. In another experiment, a small quantity of a different substance was obtained which melted at about 182° and on analysis gave numbers agreeing approximately with those required for dibromobrazilinic acid:

0·1829 gave 0·2775 CO_2 and 0·0544 H_2O. C = 41·4; H = 3·3.

$C_{19}H_{16}O_9Br_2$ requires C = 41·6; H = 2 9 per cent.

Hydrate of Brazilinic Acid, $(OMe)_3C_{13}H_6O(CO_2H)_2 \cdot CH(OH)_2$.

In the preparation of brazilinic acid by the method given in a previous paper (Trans., 1901, 79, 1410), the acid is usually obtained at once in the form of crystals melting at 208—210°.

On two occasions, however, while apparently working under the same conditions, the acid was seen to have an unusual appearance and on crystallising it from methyl alcohol, hard, pale yellow, prismatic crystals were obtained which were quite different from the crystals of brazilinic acid. The analysis of the two specimens confirmed this difference and showed that the substance is monohydrated brazilinic acid:

0·2166 gave 0·4426 CO_2 and 0·0984 H_2O. C = 55·7; H = 5·0.
0·1539 „ 0·3151 CO_2 „ 0·0690 H_2O. C = 55·8; H = 5·0.
$C_{19}H_{20}O_{10}$ requires C = 55·9; H = 4·9.

The *hydrate* of *brazilinic acid* may be dried at 100° without losing water; it melts at 130° with vigorous effervescence, then solidifies again, and if further heated the melting point is 205—208°, the melting point of brazilinic acid. If the hydrate is ground to a fine paste with a little water and then boiled with dilute sulphuric acid, the substance changes in appearance and becomes converted into a mass of fine needles which melt at 208° and consist of brazilinic acid. On analysis:

0·1217 gave 0·2605 CO_2 and 0·0506 H_2O. C = 58·4; H = 4·6.
$C_{19}H_{18}O_9$ requires C = 58·5; H = 4·6 per cent.

The basicity of the hydrate was first determined by titration with decinormal caustic soda, when 0·2741 gram required for neutralisation 0·056 gram NaOH, whereas this amount of a dibasic acid, $C_{20}H_{20}O_{10}$, should neutralise 0·054 gram NaOH.

The *silver* salt was prepared in the ordinary way by adding silver nitrate to a neutral solution of the ammonium salt; it is a white, gelatinous precipitate which, on warming, becomes crystalline and sandy and then gives numbers agreeing with those required for the silver salt of brazilinic acid:

0·2489 gave 0·3432 CO_2, 0·0617 H_2O, and 0·0866 Ag. C = 37·7; H = 2·8; Ag = 34·9.
$C_{19}H_{16}O_9Ag_2$ requires C = 37·7; H = 2·6; Ag = 35·7 per cent.

Lactone of Dihydrobrazilinic Acid, $(OMe)_3C_{13}H_6O(CO_2H)<\begin{matrix}CH_2\\CO\end{matrix}>O$.

This lactonic acid is very easily prepared by dissolving brazilinic acid in dilute caustic soda and treating the solution with excess of 3 per cent. sodium amalgam, either in a flat dish or better in a porcelain beaker fitted with a mechanical stirrer and cooled by running water On acidifying the solution, a white, amorphous precipitate, which is sometimes sticky at first but soon hardens, is thrown down; this is collected, washed well with water, and purified by recrystallisation from glacial acetic acid.

It is thus obtained as a white, apparently amorphous powder, which however, when examined under the microscope, is seen to consist of minute balls of needles. On analysis:

0·1599 gave 0·3560 CO_2 and 0·0686 H_2O. C = 60·7; H = 4·8.
0·1533 „ 0·3419 CO_2 „ 0·0662 H_2O. C = 60·8; H = 4·8.
$C_{19}H_{18}O_8$ requires C = 61·0; H = 4·8 per cent.

The *lactone* of *dihydrobrazilinic acid* melts at 227° and is very sparingly soluble in boiling water; if, however, the finely powdered substance is boiled with much water, the filtered solution, on cooling, deposits a small quantity of the acid as a crystalline powder with a satiny lustre. It is sparingly soluble in cold glacial acetic acid, benzene, or light petroleum, but dissolves readily in hot acetic acid or hot alcohol. It is very stable to permanganate at the ordinary temperature and is only very slowly oxidised even on boiling.

That this substance is a monobasic lactonic acid is very clearly shown by its behaviour towards decinormal caustic soda. 0·2444 gram was dissolved in excess of soda in the cold and the excess estimated; it was then found that 0·0332 gram NaOH had been neutralised; a monobasic acid, $C_{19}H_{18}O_{18}$, would neutralise only 0·0261 gram NaOH; obviously then, the lactone ring has undergone partial hydrolysis by treatment with cold dilute soda.

A large excess of the sodium hydroxide was now added and the solution boiled for 10 minutes, when on estimating the excess by decinormal sulphuric acid it was found that 0·0546 gram NaOH had been neutralised. If the amount of the lactonic acid taken had become dibasic it should neutralise 0·0520 gram NaOH.

The *silver* salt, $C_{19}H_{17}O_8Ag$, was prepared by adding silver nitrate to a neutral solution of the ammonium salt, and thus obtained as a white, amorphous precipitate which on analysis gave the following results:

0·202 gave 0·3467 CO_2, 0·0691 H_2O, and 0·0446 Ag. C = 46·8; H = 3·8; Ag = 22·0.
$C_{19}H_{17}O_8Ag$ requires C = 47·4; H = 3·8; Ag = 22·4 per cent.

The lactone of dihydrobrazilinic acid shows a very interesting behaviour on treatment with sulphuric acid. When the finely divided acid is mixed with sulphuric acid, it dissolves, forming an intense carmine solution; on standing, the colour rapidly becomes paler and in a few minutes the liquid is only a light yellow. Brazilinic acid also dissolves in sulphuric acid, yielding a carmine solution, but the colour does not change even on long standing (see p. 1032).

The light yellow solution of the lactonic acid in sulphuric acid deposited, after some days, a quantity of crystals, which, after draining on a porous tile, became quite white and were found to consist of a sulphuric acid compound. This substance, which is very soluble in water and is not decomposed by cold dilute sodium carbonate, is very probably a sulphate of the formula $(OMe)_3C_{13}H_6O(CO_2H)_2{\cdot}CH_2{\cdot}O{\cdot}SO_2{\cdot}OH$. If the aqueous solution of this sulphate is heated in a sealed tube at 160° for 1 hour, it is decomposed, apparently quantitatively, into the lactonic acid and sulphuric acid. The regeneratd lactonic acid, after recrystallising from acetic acid, melted at 228° and gave on analysis:

0·1445 gave 0·3216 CO_2 and 0·0688 H_2O. C = 60·7; H = 5·3.
$C_{19}H_{18}O_8$ requires C = 61·0; H = 4·8 per cent.

Lactone of Dinitrodihydrobrazilinic Acid,

$$(OMe)_3C_{13}H_4O(NO_2)_2(CO_2H)\!<\!\begin{matrix}CH_2\\CO\end{matrix}\!>\!O.$$

When the pale yellow solution of the lactone of dihydrobrazilinic acid in sulphuric acid is warmed with nitric acid, nitration takes place with formation of the above substance.

The lactone (0·2 gram) is dissolved in 3 c.c. of concentrated sulphuric acid, and as soon as the solution has become nearly colourless an equal bulk of water is added. An amount of concentrated colourless nitric acid, equal to half the volume of the solution, is now poured in, when a sage-green liquid is produced which, when heated in boiling water for about 1 minute, deposits a quantity of a crystalline substance. The precipitate, which on cooling and adding water increases somewhat in bulk, is collected on the pump, washed well, and crystallised from glacial acetic acid, in which it is very sparingly soluble. The dinitro-compound is thus obtained in microscopic balls of needles; it is very sparingly soluble in water, but dissolves readily in sodium carbonate; on heating, it decomposes with a puff and for this reason some difficulty was experienced in carrying out the analysis:

0·1479 gave 0·2630 CO_2 and 0·0473 H_2O. C = 48·5; H = 3·6.
0·1755 „ 9·7 c.c. nitrogen at 19·5 and 763 mm. N = 6·3.
$C_{19}H_{16}O_{12}N_2$ requires C = 49·1; H = 3·4; N = 6·0 per cent.

The solution of the lactone of dihydrobrazilinic acid in sulphuric acid is also readily acted on by bromine, giving at once a heavy, colourless precipitate which crystallises well from acetic acid in prismatic needles; it has not yet been further examined.

In concluding this stage of this research, the author again wishes to state that much of the heavy expense entailed has been met by repeated grants from the Government Grant Committee of the Royal Society.

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BRAZILIN AND HÆMATOXYLIN. PART V. THE OXIDATION OF TRIMETHYLBRAZILIN WITH CHROMIC ACID.

BY

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AND

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CVI.—*Brazilin and Hæmatoxylin. Part V. The Oxidation of Trimethylbrazilin with Chromic Acid.*

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Trimethylbrazilone, $C_{16}H_7O(OMe)_3(OH)_2$, which was discovered by us in 1899 (Proc., 15, 27), was first obtained by oxidising trimethylbrazilin with potassium dichromate and sulphuric acid. Trimethylbrazilin (5 grams) was ground into as fine a paste as possible with water, washed into a litre flask with 300 c.c. of water, and then 10 grams of sulphuric acid, mixed with 150 c.c. of water, added and the whole heated in a water-bath to about 70°. Potassium dichromate (7 grams dissolved in warm water) was then added in small quantities at a time, when oxidation took place rapidly, the process being complete in about 2 hours.

After filtering, the pale yellow residue was extracted with hot alcohol, which dissolved the trimethylbrazilone, leaving, as insoluble residue, a considerable quantity of a curious, amorphous, brownish-violet substance which closely resembled amorphous phosphorus in appearance. On concentrating the alcoholic solution and cooling, pure trimethylbrazilone separated in pale yellow prisms which, when rapidly heated, melted at 184—186° with decomposition. On analysis:

0·1785 gave 0·4337 CO_2 and 0·0862 H_2O. C = 66·3; H = 5·4.
0·2319 „ 0·5650 CO_2 „ 0·1096 H_2O. C = 66·4; H = 5·3.
$C_{19}H_{18}O_6$ requires C = 66·6; H = 5·3 per cent.

As the yield by this process was never more than 40 per cent. of the trimethylbrazilin employed, and often much less, a long series of experiments was made with the object of improving the method of preparation, and it was then found that a much better result, giving an almost quantitative yield, was obtained under the following conditions.

Trimethylbrazilin (50 grams) is dissolved in hot glacial acetic acid (250 grams) cooled to 15° and then chromic acid (30 grams) dissolved in a little water added in small quantities at a time. This causes a red precipitate to separate at first, but when about half the chromic acid has been added this will have dissolved, forming a red-brown solution. After each addition of the acid, the temperature rises somewhat, but is kept below 25° by cooling with water. Very shortly after the whole of the chromic acid has been added, crystallisation begins, and after standing 2 hours the whole is filtered on the pump and washed with acetic acid, when a pale yellow powder remains which weighs 35 grams and consists of nearly pure trimethylbrazilone, and in this form it melts at about 185° if rapidly heated. The mother liquor, diluted with water, deposits 15 grams of a less pure product, which, however, after extracting with a little hot alcohol, is pure enough for most purposes such as converting into acetylanhydrotrimethylbrazilone. The analysis of the trimethylbrazilone, made by this second process, gave the following results:

0·1713 gave 0·4194 CO_2 and 0·0802 H_2O. C = 66·7; H = 5·3.
0·1293 „ 0·3152 CO_2 „ 0·0645 H_2O. C = 66·5; H = 5·5.
$C_{19}H_{18}O_6$ requires C = 66·6; H = 5·3 per cent.

The melting point of the product obtained by either method, after careful recrystallisation from alcohol or acetic acid, was about 184—187°, but after one or two crystallisations from benzene the melting point had fallen to 167°; this is doubtless due to the conversion of a small quantity of the trimethylbrazilone into dehydrotrimethylbrazilone, and is evidently the reason why Herzig (*Monatsh.*, 1902, **23**, 172) gives the melting point as 160°, and Kostanecki and Lampe (*Ber.*, 1902, **35**, 1670) as 165°.

Trimethylbrazilone is almost insoluble in water, alcohol, ether, ethyl acetate, benzene, chloroform, or glacial acetic acid at the ordinary temperature, but it dissolves, although not very readily, in alcohol, benzene, or glacial acetic acid on boiling. It is insoluble in sodium carbonate or in caustic potash solution in the cold, but the finely powdered substance dissolves in hot potash solution forming a yellow liquid from which acids, and even carbon dioxide, precipitate a white, amorphous substance, which, after recrystallisation, melts at 197° and consists of anhydrotrimethylbrazilone. Herzig (*Monatsh.*, 1901, **22**, 10) has investigated the action of potash on trimethylbrazilone quantitatively and finds that 1 mol. is capable of neutralising exactly 1 mol. of potassium hydroxide; he also finds that the solution, when acidified, yields anhydrotrimethylbrazilone.

That trimethylbrazilone still contains the three methoxy-groups of

the original trimethylbrazilin was proved by direct determination, which gave the following result:

0·2527 gave 0·5368 AgI. MeO = 28·0.
$C_{16}H_9O_3(OMe)_3$ requires MeO = 27·2 per cent.

Examination of the Chromium Liquors from the Preparation of Trimethylbrazilone.

The aqueous chromium liquors from the oxidation of trimethylbrazilin with potassium dichromate and sulphuric acid were saturated with ammonium sulphate and repeatedly extracted with ether. The ethereal solution was washed with water, dried over calcium chloride, and evaporated, when a considerable quantity of a thick, dark brown oil was obtained, which, on standing, partially solidified. The whole was boiled with much water and filtered (the black, insoluble, resinous residue being discarded), the filtrate was mixed with a large excess of lead acetate, allowed to stand until nearly cold, and the very voluminous red salt, which had settled out, collected on the pump and thoroughly washed. The filtrate from the lead salt was evaporated to a small bulk and extracted about twenty times with ether; the ethereal solution was then washed until free from acetic acid, dried over calcium chloride, and concentrated. After standing for a few days, a considerable quantity of a colourless, crystalline crust had separated; this, after crystallisation from acetic acid, melted at 155—156° and consisted of m-*meconine*. On analysis:

0·1245 gave 0·2821 CO_2 and 0·0586 H_2O. C = 61·8; H = 5·2.
$C_{10}H_{10}O_4$ requires C = 61·8; H = 5·1 per cent.

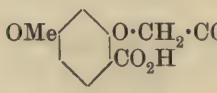
The substance was insoluble in sodium carbonate but soluble in caustic soda, and it showed all the properties of the *m*-meconine described in the previous paper (this vol., p. 1027). Moreover, an intimate mixture of both samples melted at 155°, and therefore there could be no doubt as to their identity. This formation of *m*-meconine by the direct oxidation of trimethylbrazilin is a matter of considerable importance.

Examination of the Lead Salt.—The lead salt was ground up into a fine paste with much water and decomposed by sulphuretted hydrogen, first in the cold, and then on the water-bath. After filtering, the filtrate and washings of the lead sulphide were evaporated nearly to dryness, when a thick, brown syrup was left which after a time partially solidified. From this uninviting mass, by again treating with lead acetate and a subsequent tedious series of fractional crystallisations, three acids were

isolated in a pure condition melting at 215° with vigorous decomposition, at 174°, and at 190° respectively.

The first of these was found, on fusion with potash, to be derived from the resorcyl nucleus of brazilin, and is evidently identical with the *methoxycarboxyphenoxylactic acid* described in the previous paper (this vol., p. 1030), but the quantity available was too small for analysis.

The acid melting at 174° is 2-carboxy-5-methoxyphenoxyacetic acid,



an acid which has already been isolated from among the products of the oxidation of trimethylbrazilin with permanganate (Trans., 1901, **79**, 1407). On analysis:

0·1417 gave 0·2740 CO_2 and 0·0578 H_2O. C = 52·7; H = 4·5.
$C_{10}H_{10}O_6$ requires C = 53·1; H = 4·4 per cent.

The acid melting at 190°, and which was obtained in the largest quantity, was easily identified as *m*-hemipinic acid.

A specimen purified by repeated recrystallisation from water with the aid of animal charcoal, was analysed with the following results:

0·1214 gave 0·237 CO_2 and 0·049 H_2O. C = 53·2; H = 4·5.
$C_{10}H_{10}O_6$ requires C = 53·1; H = 4·4 per cent.

Anhydrotrimethylbrazilone, $C_{16}H_6O(OMe)_3 \cdot OH$.

When trimethylbrazilone is heated a few degrees above its melting point, it loses water and is converted into *anhydrotrimethylbrazilone*:

$$C_{16}H_8O_2(OMe)_3 \cdot OH = C_{16}H_6O(OMe)_3 \cdot OH + H_2O.$$

In carrying out this decomposition, trimethylbrazilone in quantities of about 0·5 gram is heated cautiously in a test-tube over a bunsen flame; the substance first melts, then gives off aqueous vapour, and, on cooling, the residue sets to a dark coloured, transparent resin. This is dissolved in acetic acid, from which the new substance separates in small crystals, which, after repeated recrystallisation, become almost colourless.

Another way of obtaining the anhydro-compound is to boil trimethylbrazilone with alcoholic potash, when it first dissolves and then soon begins to deposit crystals. After standing for some time and acidifying, these are collected and crystallised from acetic acid.

The anhydrotrimethylbrazilone obtained by the above two methods gave on analysis the following results:

I. 0·2069 gave 0·5331 CO_2 and 0·0896 H_2O. C = 70·3; H = 4·8.
II. 0·1451 „ 0·3739 CO_2 „ 0·0638 H_2O. C = 70·3; H = 4·9.
$C_{19}H_{16}O_5$ requires C = 70·4; H = 4·9 per cent.

The best method of preparing anhydrotrimethylbrazilone is, however, by the hydrolysis of the acetyl compound described in the next section. The acetate (3 grams) is mixed with a solution of potash (2 grams) in methyl alcohol (50 c.c.) and heated to boiling for 10 minutes on the water-bath, when the crystals soon dissolve, and if about half the methyl alcohol is then allowed to evaporate off over sulphuric acid in a vacuum desiccator, colourless, warty masses gradually separate which evidently consist of the *potassium* compound of anhydrotrimethylbrazilone, $C_{19}H_{15}O_5K$. The separation does not take place nearly so well as in the case of the corresponding potassium compound of anhydrotetramethylhæmatoxylone (this vol., p. 1063), owing to the latter potassium compound being much less soluble in methyl alcohol than the former. The crystals were, however, collected on the pump, washed rapidly with methyl alcohol, and analysed, when results were obtained which agreed only approximately with those required for the potassium compound:

0·4020 gave 0·1045 K_2SO_4. K = 11·2.
$C_{19}H_{15}O_5K$ requires K = 10·7 per cent.

This potassium compound becomes greenish when exposed to the air, and it is slowly decomposed by water, but much more rapidly by mineral acids, and even carbonic acid, with separation of anhydrotrimethylbrazilone. The pale green methyl alcoholic mother liquors of this potassium compound, on the addition of water, at first give no precipitate, but on standing, glistening crystals gradually separate. After about two hours, the crystals were collected, washed with water, and found to consist of pure anhydrotrimethylbrazilone, but only a small amount of the potassium salt had been decomposed, and on acidifying the filtrate a large further precipitate was obtained.

In the actual preparation of anhydrotrimethylbrazilone, the product of the hydrolysis of the acetate is simply poured into excess of dilute hydrochloric acid and the precipitate recrystallised from acetic acid.

Anhydrotrimethylbrazilone melts at 198° and is readily soluble in hot alcohol, from which it separates on cooling in slightly brownish-coloured, iridescent plates; it is sparingly soluble in boiling benzene or light petroleum, and very readily so in acetone. It is insoluble in sodium carbonate and in ammonia, but dissolves appreciably in hot, strong potash solution evidently with formation of the salt described above.

Acetylanhydrotrimethylbrazilone, $C_{16}H_6O(OMe)_3{\cdot}O{\cdot}C_2H_3O$.

This substance, which was first obtained by Herzig (*Monatsh.*, 1895, **16**, 913) by the oxidation of acetyltrimethylbrazilin, is readily prepared by heating trimethylbrazilone with acetic anhydride and sodium acetate, when elimination of water and acetylation take place at the same time. Trimethylbrazilone (10 grams) is heated with acetic anhydride (40 grams) and fused sodium acetate (5 grams) for one hour to boiling when, on cooling, a mass of crystals separates. The product is mixed with water and allowed to stand until the excess of acetic anhydride has been decomposed; the crystals are then collected and recrystallised from acetic acid containing a little acetic anhydride or from benzene. Thus obtained, the substance melts at 174—175° as stated by Herzig. On analysis:

0·2282 gave 0·5768 CO_2 and 0·099 H_2O. C = 68·9; H = 4·9.
$C_{21}H_{18}O_6$ requires C = 68·8; H = 4·9 per cent.

Acetylanhydrotrimethylbrazilone is readily soluble in acetic acid, benzene, or acetone, but only sparingly so in most other organic solvents in the cold. That it contains only one acetyl group was shown by boiling it with dilute sulphuric acid, distilling the product in steam, and estimating the acetic acid in the distillate with decinormal caustic soda, when 0·2092 gram yielded 0·0338 gram of acetic acid, or 16·2 per cent. A substance of the formula $C_{21}H_{18}O_6$, containing one acetyl group, would yield 16·4 per cent. of acetic acid on hydrolysis.

The residue in the distilling flask, after crystallisation from acetic acid, melted at 175° and consisted of pure anhydrotrimethylbrazilone.

Oxidation of Anhydrotrimethylbrazilone with Permanganate. Formation of m-*Hemipinic Acid*, $(CO_2H)_2C_6H_2(OMe)_2$, *and Dimethoxycarboxybenzoylformic Acid*, $CO_2H{\cdot}CO{\cdot}C_6H_2(OMe)_2{\cdot}CO_2H$.

In carrying out this oxidation, pure anhydrotrimethylbrazilone (prepared from the acetate) was ground to a fine paste with water, and treated with permanganate at the ordinary temperature until the colour remained permanent overnight, which was the case after about three days. Oxidation takes place readily at first with evolution of some heat, so that in order to avoid the temperature rising above 20° cooling with water is necessary. The excess of permanganate is destroyed with sodium sulphite, the whole heated to boiling, and the filtrate and washings of the manganese precipitate evaporated nearly to dryness, acidified, and extracted 20 times with ether. The ethereal solution, after drying over calcium chloride, was concentrated to a small bulk and left standing in a closed flask for two days, when a small

quantity of a dark-coloured, crystalline substance had separated; this was washed with ether, dissolved in dilute sodium carbonate, and boiled with purified animal charcoal. A clear solution was then concentrated and acidified, when, on standing, hard, nearly colourless prisms gradually formed; these melted at about 190° with effervescence and consisted of *m*-hemipinic acid.

0·1533 gave 0·2992 CO_2 and 0·0665 H_2O. C = 53·2; H = 4·8.
$C_{10}H_{10}O_6$ requires C = 53·1; H = 4·4 per cent.

The ethereal solution which had been decanted from the crude *m*-hemipinic acid as described above, was evaporated, when a pale yellow syrup was obtained which gradually became semi-solid. In contact with porous porcelain, the oily impurity was soon completely absorbed, and, on allowing the solution of the nearly colourless residue in water to concentrate slowly over sulphuric acid, an acid crystallised in hard glistening prisms. This was collected, washed with a little water, and dried in the water-oven; the substance first became sticky, then hard again, and when quite dry the melting point was about 150°.

On analysis:

0·1323 gave 0·2484 CO_2 and 0·0485 H_2O. C = 51·2; H = 4·1.
$C_{11}H_{10}O_7$ requires C = 52·0; H = 3·9 per cent.

That this acid is *dimethoxycarboxybenzoylformic acid* was shown by a direct comparison with a sample of this acid which had been obtained from trimethylbrazilin by a different process (this vol., p. 1023). It appears that this acid is the principal product of the oxidation of anhydrotrimethylbrazilone.

The aqueous solution of the oxidation product which had been treated with ether as described above was evaporated to dryness, mixed with sand, and extracted with ether in a Soxhlet apparatus. The extract, on evaporation, deposited a small quantity of an oil which solidified almost completely, and consisted of a mixture of dimethoxycarboxybenzoylformic acid with some oxalic acid, but the latter was present only in small quantity.

Action of Phenylhydrazine on Trimethylbrazilone. Formation of Deoxytrimethylbrazilone, $C_{19}H_{18}O_4$.

When trimethylbrazilone is heated with phenylhydrazine, a vigorous evolution of gas takes place and the product smells strongly of ammonia. The reaction may be moderated by dissolving trimethylbrazilone in acetic acid at 40—50° and adding excess of phenylhydrazine; the temperature rises somewhat, a little gas is given off, and on standing a quantity of crystals separate. These after washing with acetic acid melt at 172—173°.

The best way of preparing this substance, however, is to heat together trimethylbrazilone (3 grams), phenylhydrazine (6 grams), and alcohol (30 grams) on the water-bath. The crystals soon dissolve and if the yellow solution is poured in a thin stream into very dilute hydrochloric acid, an ochreous precipitate separates which is collected on the pump and well washed with dilute hydrochloric acid. The substance, which smells strongly of benzene, is drained on a porous plate and then warmed with a little alcohol at 50° for a few minutes by which means most of the dark coloured impurities pass into the alcohol, leaving the deoxytrimethylbrazilone undissolved. After allowing to cool and filtering on the pump, the precipitate is washed with alcohol and then crystallised from much boiling alcohol. The satiny mass of crystals thus obtained contains no nitrogen, as was proved, not only by the usual qualitative test, but also by an experiment conducted exactly as in the determination of nitrogen, but which yielded no gas. The analyses of three different specimens of this remarkable substance gave the following results:

0·1466 gave 0·3964 CO_2 and 0·0786 H_2O. C = 73·7; H = 5·9.
0·1344 „ 0·3565 CO_2 „ 0·0665 H_2O. C = 73·6; H = 5·8.
0·1567 „ 0·4230 CO_2 „ 0·0827 H_2O. C = 73·6; H = 5·8.
$C_{19}H_{18}O_4$ requires C = 73·6; H = 5·8 per cent.

Deoxytrimethylbrazilone is therefore formed by the removal of two atoms of oxygen from trimethylbrazilone,

$$C_{19}H_{18}O_6 - 2O = C_{19}H_{18}O_4,$$

the phenylhydrazine having acted as a reducing agent.

It melts at about 173° and is sparingly soluble in ether, light petroleum, cold alcohol, or acetic acid, but dissolves readily in acetone, hot benzene, or chloroform and fairly easily in boiling alcohol, and crystallises from these solvents in almost colourless needles. It is quite insoluble in potash, even on boiling; concentrated hydrochloric acid colours it yellowish-red and, on boiling, the crystals dissolve and then decomposition sets in with separation of an oil. It dissolves in sulphuric acid with a dark orange colour, and when the solution is heated on the water-bath for two minutes it acquires a striking yellow fluorescence, and on adding water a brown precipitate separates which is soluble in warm water.

Concentrated nitric acid dissolves the substance with an intense purple colour and on adding water a purple precipitate separates. Boiling with 50 per cent. nitric acid also gives a magnificent purple solution, oxidation taking place only with difficulty.

Deoxytrimethylbrazilone dissolves in hot acetic anhydride, forming a dark reddish-brown solution, and if, after boiling for five minutes,

the liquid is poured into a basin, crystallisation commences at once and the crystals, after collection on the pump and washing with acetic anhydride, melt at about 173° and consist of the unchanged substance. On analysis:

0·1338 gave 0·3594 CO_2 and 0·0717 H_2O. C = 73·3; H = 5·9.
$C_{19}H_{18}O_4$ requires C = 73·5; H = 5·8 per cent.

This shows that the substance cannot contain a hydroxy-group.

Deoxytrimethylbrazilone is readily attacked by permanganate, but although many experiments have been made under different conditions, it has not been found possible to isolate any decomposition products of interest from the product of the oxidation.

Working at the ordinary temperature under exactly the same conditions as used in the case of the oxidation of anhydrotrimethylbrazilone (p. 1045), large quantities of oxalic acid and acetic acid are produced and only traces of other oxidation products.

Nitrohydroxydihydrotrimethylbrazilone, $NO_2 \cdot C_{16}H_9O_3(OMe)_3 \cdot OH$.

This remarkable substance is produced by the action of nitric acid on trimethylbrazilone, according to the following equation:

$$C_{19}H_{18}O_6 + HNO_3 = C_{19}H_{19}O_9N,$$

nitration and addition of water taking place simultaneously.

In our first experiments, this substance was always prepared by treating trimethylbrazilone with dilute nitric acid under the following conditions. Trimethylbrazilone (2 grams) was ground to a very fine paste with a little water, mixed with about 80—100 c.c. of dilute nitric acid (containing 1 vol. of nitric acid of sp. gr. 1·42 to 2 vols. of water), and rapidly heated to about 50° over a free flame. The almost colourless mixture first assumed a deep yellow colour and, as the temperature increased, rapidly deposited a pale yellow, very voluminous substance, very little oxidation and evolution of red fumes taking place. The whole experiment only takes a few minutes.

After standing until cold, the product was mixed with its own volume of water, the precipitate collected on the pump, well washed with water, and recrystallised from glacial acetic acid. The lemon-yellow crystals thus obtained are frequently not quite pure, and contain traces of trimethylbrazilone which have escaped the action of the nitric acid; the latter is easily removed by extracting the crystalline mass with boiling toluene, which dissolves the impurity easily, but in which the nitro-compound is practically insoluble. After filtering, the residue was once more crystallised from glacial acetic acid, and then analysed, with the following result:

0·1390 gave 0·2868 CO_2 and 0·0612 H_2O. C = 56·2; H = 4·9.
0·2144 „ 0·4401 CO_2 „ 0·0942 H_2O. C = 56·0; H = 4·9.
0·1942 „ 6·3 c.c. nitrogen at 14° and 760 mm. N = 3·8.
$C_{19}H_{19}O_9N$ requires C = 56·3; H = 4·7; N = 3·5 per cent.

This method of preparation gives at once a very pure product, but it is not quite so convenient as the following modification, which was subsequently adopted in preparing large quantities of the nitro-compound.

Nitric acid (ordinary concentrated, 50 c.c.)* is placed in a quarter-litre flask and then very finely powdered trimethylbrazilone (10 grams) added in small quantities at a time, any rise of temperature being carefully checked by cooling the flask with water. The substance dissolves in the acid, and when, after standing for 10 minutes, water is added, a yellowish-green, voluminous precipitate separates, which is collected on the pump, well washed with water, and left in contact with porous porcelain in a dark place. The mass is then crystallised from acetic acid, extracted with boiling toluene, and again crystallised from acetic acid, exactly as explained in the case of the previous preparation. The pale yellow needles thus obtained gave on analysis:

0·1926 gave 0·3993 CO_2 and 0·0849 H_2O. C = 56·5; H = 4·9.
0·1901 „ 5·9 c.c. nitrogen at 16° and 750 mm. N = 3·5.
$C_{19}H_{19}O_9N$ requires C = 56·3; H = 4·7; N = 3·5 per cent.

Nitrohydroxydihydrotrimethylbrazilone, when heated in a capillary tube, darkens at 225° and melts at about 230° with decomposition. It is very sparingly soluble in alcohol and glacial acetic acid in the cold and dissolves with difficulty even on boiling; it is almost insoluble in boiling benzene, or toluene, in light petroleum, or in water. It is insoluble in dilute sodium carbonate in the cold, but on boiling it gradually dissolves, yielding a deep violet solution; in caustic soda, it dissolves at once, forming an intense violet solution which, on standing, soon loses its colour and deposits a drab precipitate (see p. 1050). Preparations of this nitro-compound must be kept in the dark, since the pale yellow crystals, when exposed to sunlight, rapidly become an intense yellow. It dissolves in concentrated sulphuric acid with a brown colour, and on diluting somewhat and heating an intense indigo-blue solution is produced, which, on the addition of alcohol, becomes deep violet.

The molecular weight of the nitro-compound, determined by the boiling point method in glacial acetic acid solution, gave 367 and 371,

* Bollina, Kostanecki, and Tambor (*Ber.*, 1902, **35**, 1676) use nitric acid of sp. gr. 1·3 in preparing this nitro-compound, and state that the substance, simply crystallised from alcohol and acetic acid, melts at 225°.

whereas the mol. wt. of $C_{19}H_{19}O_9N$ is 405. The methoxy-groups were also determined, with the following result:

0·3812 gave 0·6546 AgI. MeO = 22·7.

$C_{16}H_{10}O_6N(OMe)_3$ requires MeO = 22·9 per cent.

Nitroacetoxydihydrotrimethylbrazilone, $NO_2 \cdot C_{16}H_9O_3(OMe)_3 \cdot O \cdot C_2H_3O$, is very easily obtained by boiling the nitro-compound with eight times its weight of acetic anhydride for 10 minutes and leaving the solution over solid potash in a vacuum desiccator. The acetyl compound soon begins to separate in crusts of warty crystals, and, on the following day, these are collected, washed with acetic anhydride, and dried at 100°. On analysis:

0·1709 gave 0·3564 CO_2 and 0·0736 H_2O. C = 56·8; H = 4·7.
0·1413 „ 0·2922 CO_2 „ 0·0614 H_2O. C = 56·4; H = 4·8.
0·1956 „ 5·5 c.c. nitrogen at 20° and 760 mm. N = 3·2.

$C_{21}H_{21}O_{10}N$ requires C = 56·4; H = 4·7; N = 3·1 per cent.

Nitroacetoxydihydrotrimethylbrazilone melts at 150—155° with previous softening, and crystallises from acetic acid in round, warty masses. When ground to a paste with water, it gives no immediate coloration with dilute caustic potash, but on standing it gradually dissolves, forming a purple solution. When warmed with potash, it dissolves at once with a purple colour.

That this substance is a monoacetyl compound was proved by hydrolysing it with decinormal sulphuric acid and, after filtering from the insoluble nitrohydroxy-compound, estimating the amount of acetic acid by titration with decinormal caustic soda. It was found that the acetic acid from 0·558 gram of substance neutralised 0·045 gram NaOH, whereas, on the assumption that the substance is a monoacetyl compound of the formula $C_{21}H_{21}O_{10}N$, the amount neutralised should have been 0·049 gram NaOH. The nitrohydroxy-compound obtained during this experiment crystallised from acetic acid in almost colourless needles which melted at 228—230°.

Action of Potash on Nitrohydroxydihydrotrimethylbrazilone.

It has already been stated (p. 1049) that this nitro-compound dissolves in potash with an intense purple colour and that, on standing, this gradually disappears and a drab precipitate is deposited.*

This important decomposition was made the subject of an extended investigation, and it was ultimately found that the best yield of the various products formed was obtained under the following conditions.

* If, however, the potash solution employed is very weak, and only in slight excess, the violet colour changes to brown *without any precipitate being formed*: the course of the reaction in this case is being investigated.

The nitro-compound (3 grams) is ground up to a fine paste with about 10 c.c. of water, then 25 c.c. of 50 per cent. potash solution are added and the whole well shaken to ensure complete solution, any tendency to rise of temperature, which is usually noticeable, being checked by cooling with water. After about 10 minutes, the purple colour will have disappeared, the whole is then diluted with water, filtered on the pump, the precipitate washed with water and dried on porous porcelain, it then weighed 1·0—1·2 grams. The well-powdered substance is now boiled with alcohol, which dissolves about two-thirds, filtered, and the residue, which is pale ochre-coloured, washed several times with hot alcohol, in which it is practically insoluble. The substance is then purified by crystallisation from much toluene, from which it separates in almost colourless, microscopic needles of melting point 205°. On analysis:

0·1498 gave 0·3033 CO_2 and 0·0711 H_2O. C = 55·2; H = 5·3.
0·1546 „ 0·3133 CO_2 „ 0·0721 H_2O. C = 55·1; H = 5·1.
0·1738 „ 10·6 c.c. of nitrogen at 16° and 769 mm. N = 7·2.

$C_9H_{11}O_4N$ requires C = 54·8; H = 5·6; N = 7·1 per cent.
$(C_9H_{10}O_4N)_2$ „ C = 55·1; H = 5·1; N = 7·2 „ „
$C_9H_9O_4N$ „ C = 55·4; H = 4·6; N = 7·2 „ „

That this substance contains two methoxy-groups, and is therefore a derivative of the catechol nucleus of brazilin, is shown by the following determination by Zeisel's method.

0·1506 gave 0·3783 AgI. MeO = 32·2.

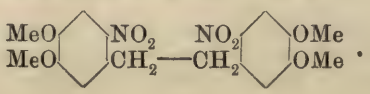
$C_7H_5O_2N(OMe)_2$ requires MeO = 31·6 per cent.

The dark coloured hydriodic acid from this determination deposited, after some days, a brown, crystalline substance, which was collected, washed with a little very dilute sulphurous acid, and left in contact with porous porcelain until dry.

This substance dissolves readily in methyl alcohol and on diluting and shaking with air a deep blue solution is produced.

The addition of ferric chloride to the methyl alcoholic solution gives an intense indigo-blue colour which becomes reddish-violet on the addition of more of the reagent, and a precipitate is formed. The methyl alcoholic solution of the substance gives a greenish-white, insoluble precipitate with lead acetate.

Although the evidence is not sufficient to definitely establish the nature of the nitro-compound of melting point 205°, it seems probable, for reasons explained in the previous paper (this vol., p. 1021), that it is a dinitrodimethylhomocatechol of the formula



The dark brown alcoholic extract obtained in the first purification of the substance of melting point 205° contains a second product of the action of potash on nitrohydroxydihydrotrimethylbrazilone. In order to isolate this, the dark solution is digested with animal charcoal for 1 hour, evaporated to a small bulk, and mixed with an equal volume of hot water, when, on standing, brown, leafy crystals separate which, on repeated recrystallisation, are obtained almost colourless and melt at 118°. On analysis:

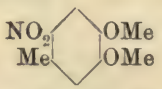
0·1393 gave 0·2804 CO_2 and 0·0736 H_2O. C = 54·9; H = 5·9.
0·1381 „ 0·2790 CO_2 „ 0·0711 H_2O. C = 55·1; H = 5·7.
0·1753 „ 10·6 c.c. of nitrogen at 15° and 768 mm. N = 7·2.
$C_9H_{11}O_4N$ requires C = 54·8; H = 5·6; N = 7·1 per cent.

This substance is sparingly soluble in cold alcohol or light petroleum, and almost insoluble in cold water. It dissolves, however, in much boiling water, separating again in slender needles, and, indeed, the substance, if very dark coloured, as is often the case, is best purified in this way. It is quite insoluble in potash solution, but dissolves in sulphuric acid with a deep orange colour.

That this substance contains two methoxy-groups, and is therefore, like the substance of melting point 205°, derived from the catechol nucleus of brazilin, is shown by the following determination by Zeisel's method:

0·1674 gave 0·4062 AgI. MeO = 31·9.
$C_7H_5O_2N(OMe)_2$ requires MeO = 31·6 per cent.

The consideration of the percentage composition and properties of this substance leave scarcely any doubt that it is identical with the *nitrodimethylhomocatechol* of the formula



which H. Cousin (*Ann. Chim. Phys.*, 1898, [vii], **13**, 480) obtained direct from homocatechol by nitration and subsequent methylation of the 6-nitrohomocatechol, $C_6H_2Me(OH)_2{\cdot}NO_2$ [1 : 3 : 4 : 6], produced. Cousin gives the melting point of his substance as 117°.

The deep brown potash solution which had been separated from the mixed substances (m. p. 205° and 118°) as described above (p. 1051) was acidified and allowed to stand, and the almost black, resinous mass which was deposited collected and washed with water.

From this uninviting mass, by repeated treatment with water and animal charcoal, a considerable quantity of an almost colourless substance was obtained which crystallised from water in needles, melted at 155° and gave, with ferric chloride, an intense violet coloration.

That this substance is p-*methoxysalicylic acid* was proved by a direct comparison with a sample of this acid prepared by the methylation of resorcylic acid. It was also analysed with the following results:

0·1952 gave 0·4095 CO_2 and 0·0848 H_2O. C = 57·2; H = 4·8.
$C_8H_8O_4$ requires C = 57·1; H = 4·8 per cent.

The aqueous liquors from the crude *p*-methoxysalicylic acid were distilled in steam, the acid distillate boiled with barium carbonate, filtered, and the filtrate evaporated to dryness.

The residue, which was considerable, consisted mainly of barium formate, since its solution in water blackened silver nitrate and reduced mercuric to mercurous chloride; also CO was evolved with sulphuric acid. From this it follows that *formic acid* is one of the products of the action of potash on nitrohydroxydihydrotrimethylbrazilone.

Action of Phenylhydrazine on Nitrohydroxydihydrotrimethylbrazilone.

In studying this reaction, the nitro-compound, in quantities of not more than 2 grams, is warmed with a little acetic acid (20 grams) to about 20° and then carefully purified phenylhydrazine (3 grams) is added, when the solid soon dissolves, forming a dark brownish-red solution. This is filtered from any undissolved substance, if necessary, and allowed to stand, when crystallisation soon sets in, the whole ultimately becoming a pasty mass of crystals. These are collected on the pump, washed thoroughly with glacial acetic acid, and drained on a porous plate. If the operation has been successful, the product will be a yellowish-red, crystalline mass and not dark red and gelatinous in appearance, as is often the case if the temperature has been allowed to rise too high during the preparation. After drying at 100°, the following results were obtained on analysis:

0·1534 gave 0·3619 CO_2 and 0·0770 H_2O. C = 64·3; H = 5·6.
0·1683 „ 0·3978 CO_2 „ 0·0848 H_2O. C = 64·4; H = 5·6.
0·1347 „ 19·6 c.c. of nitrogen at 22° and 761 mm. N = 16·0.
$C_{24}H_{25}O_4N_5$ requires C = 64·4; H = 5·6; N = 15·7 per cent.

This interesting substance, the constitution of which is not yet understood, melts at about 170° and dissolves in sulphuric acid with an olive green colour, but is insoluble in alkalis. It is sparingly soluble in glacial acetic acid in the cold, but dissolves readily on boiling, forming a pale yellow solution from which it separates on cooling as an orange-red, gelatinous mass. It is readily soluble in acetone and hot benzene, forming pale yellow solutions, but is insoluble in light petroleum. When heated with acids, it resinifies and for this reason it has, so far, not been found possible to remove the phenylhydrazine

residues and determine the nature of the parent substance. Its stability towards acids is, however, well shown by the fact that it dissolves in 20 per cent. alcoholic hydrochloric acid, and if after 2 hours an equal bulk of water is added, the unchanged substance gradually crystallises from the solution. As the determination of the nature of this compound is of the first importance in connection with the constitution of brazilin, its investigation is being continued. The dark coloured acetic acid mother liquors of the above substance gave, on diluting with water, an ochreous precipitate which was collected, washed well, and boiled with sodium carbonate. The hot liquid was filtered from the black resin which had separated, decolorised as far as possible with animal charcoal, and acidified, when a bulky precipitate was obtained which crystallised from water in colourless needles and melted at 155°. On analysis:

0·1264 gave 0·2647 CO_2 and 0·0567 H_2O. C = 57·1; H = 5·0.
$C_8H_8O_4$ requires C = 57·1; H = 4·8 per cent.

This acid is *p*-methoxysalicylic acid, $MeO{\cdot}C_6H_3(OH){\cdot}CO_2H$, since its alcoholic solution gives, with ferric chloride, an intense violet coloration, and when mixed with a sample of this acid, prepared by the methylation of β-resorcylic acid, there was no lowering of the melting point.

Action of p-*Bromophenylhydrazine on Nitrohydroxydihydrotrimethylbrazilone.*

Owing to the remarkable nature of the reaction just described and the peculiar properties of the phenylhydrazine compound obtained, it was thought advisable to study the action of *p*-bromophenylhydrazine on the nitro-compound in order to obtain a check on the composition of the condensation product.

Carefully purified nitrohydroxydihydrotrimethylbrazilone was therefore treated with *p*-bromophenylhydrazine, in acetic acid solution, substantially as described above, and the orange-red crystals which separated were collected and thoroughly washed with acetic acid. Two preparations were made and analysed separately:

I. 0·1861 gave 0·3228 CO_2 and 0·068 H_2O. C = 47·3; H = 4·0.
0·1475 „ 15 c.c. of nitrogen at 15° and 764 mm. N = 11·9.
0·2822 „ 0·1794 AgBr. Br = 27·0
II. 0·1470 „ 0·2568 CO_2 and 0·0518 H_2O. C = 47·6; H = 3·9.
0·2171 „ 22·6 c.c. of nitrogen at 19° and 752 mm. N = 11·8.
0·2538 „ 0·1593 AgBr. Br = 26·7.

$C_{24}H_{23}O_4N_5Br_2$ requires C = 47·6; H = 3·8; N = 11·6; Br = 26·4 per cent.

This substance has no definite melting point and when heated in a

capillary tube it shrinks together at about 195° and decomposes at 220°. It is readily soluble in hot glacial acetic acid and crystallises on cooling in microscopic groups of orange needles.

It will be seen from the above analyses that the substance $C_{24}H_{23}O_4N_5Br_2$ corresponds exactly with the substance $C_{24}H_{25}O_4N_5$ obtained by the action of phenylhydrazine on the nitro-compound.

Oxidation of Nitrohydroxydihydrotrimethylbrazilone.

In this oxidation, the nitro-compound was employed in the form in which it is precipitated by pouring the product of the action of nitric acid on trimethylbrazilone into water, as in this condition it is much more readily oxidised than after recrystallisation. The substance was ground to a fine paste with water and oxidised with permanganate at 25—30° until, after standing for four hours, the colour remained permanent. After removing the excess of permanganate with sodium sulphite, the whole was filtered on the pump, the precipitate washed well, and the deep yellow, alkaline filtrate evaporated to a small bulk and acidified, when a considerable quantity of a black, resinous substance separated. The whole was extracted with ether, the ethereal solution dried over calcium chloride, and evaporated to a small bulk, when, on standing for some days, a quantity of a crystalline substance had separated. This was collected, washed with ether, and repeatedly recrystallised from water with the aid of animal charcoal, when nearly colourless, slender needles were obtained which gave on analysis the following results:

0·1274 gave 0·2486 CO_2 and 0·0528 H_2O. C = 53·2; H = 4·6.

$C_{10}H_{10}O_6$ requires C = 53·1; H = 4·4 per cent.

This acid melted at 170—172°, was dibasic, and on fusion with potash yielded a substance which gave a violet coloration with ferric chloride. The analysis and these properties point to the acid being 2-carboxy-5-methoxyphenoxyacetic acid,

$$MeO\cdot C_6H_3(CO_2H)\cdot O\cdot CH_2\cdot CO_2H,$$

and that this was the case was proved by mixing a small quantity with a specimen of this acid which had been obtained from brazilin by another method when no lowering of the melting point could be observed. As the formation of this acid is of great importance in deciding the constitution of nitrohydroxydihydrotrimethylbrazilone, the experiment is being repeated with very carefully purified substance, but unfortunately the oxidation then takes place with extreme slowness.

Examination of the Nitric Acid Liquors from the Preparation of Nitrohydroxydihydrotrimethylbrazilone.

The accumulated mother liquors from a large number of preparations of the nitro-compound were saturated with ammonium sulphate and repeatedly extracted with ether. The etheral solution was dried over calcium chloride, evaporated to a small bulk, and then allowed to concentrate further in the air, when deep yellow crystals separated which were collected and left in contact with porous porcelain until quite free from oily mother liquor. The residue was then crystallised from boiling water, from which it separated in almost colourless needles. On analysis:

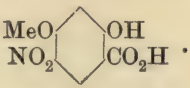
0·1768 gave 0·2074 CO_2 and 0·0402 H_2O. C = 44·6; H = 3·5.
0·2152 „ 11·8 c.c. nitrogen at 18° and 770 mm. N = 6·4.
$C_8H_7O_6N$ requires C = 45·1; H = 3·3; N = 6·5.

This nitro-acid melts at about 230° with decomposition (after softening at 220°), is sparingly soluble in water, and gives with ferric chloride a blood-red coloration. As the analysis and properties seemed to show that this substance was nitromethoxysalicylic acid, $MeO{\cdot}C_6H_2(OH)(NO_2){\cdot}CO_2H$, this hitherto unknown acid was prepared and found to be identical with the acid just described.

p-Methoxysalicylic acid was dissolved in a little warm glacial acetic acid, mixed with concentrated nitric acid, and warmed until a vigorous action commenced; the tube containing the mixture was then immediately plunged into cold water. The crystals which separated were collected, washed with a little acetic acid, and crystallised from water, when pale yellow, microscopic prisms were obtained which melted at about 230°. On analysis:

0·2848 gave 16·3 c.c. of nitrogen at 19° and 757 mm. N = 6·5.
$C_8H_7O_6N$ requires N = 6·5 per cent.

The constitution of this nitromethoxysalicylic acid is probably that represented by the formula



The authors wish to express their thanks to Messrs. J. Yates and D. T. Jones for valuable assistance in carrying out these experiments.

The Owens College,
Manchester.

RICHARD CLAY AND SONS, LIMITED, LONDON AND BUNGAY

BRAZILIN AND HÆMATOXYLIN. PART VI. THE OXIDATION OF TETRAMETHYLHÆMATOXYLIN WITH CHROMIC ACID.

BY

W. H. PERKIN, JUN.

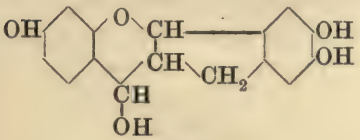
From the Transactions of the Chemical Society, 1902. Vol. 81.

CVII.—*Brazilin and Hæmatoxylin. Part VI. The Oxidation of Tetramethylhæmatoxylin with Chromic Acid.*

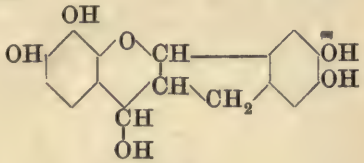
By W. H. Perkin, jun.

It has already been shown (Trans., 1902, 81, 237) that the comparison of the behaviour of trimethylbrazilin and tetramethylhæmatoxylin on oxidation with permanganate has brought out in the clearest way the great similarity in the constitution of the two natural colouring matters brazilin and hæmatoxylin, and has proved that, whereas both are derivatives of catechol, brazilin contains also a resorcinol nucleus which, in the case of hæmatoxylin, gives place to the pyrogallol nucleus.

The relationship between these two substances has been expressed by the author by means of the formulæ

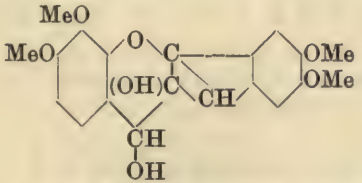


Brazilin.



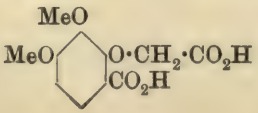
Hæmatoxylin.

When submitted to oxidation with chromic acid, tetramethylhæmatoxylin again shows a behaviour exactly similar to that of trimethylbrazilin, yielding, as it does, in the first place *tetramethylhæmatoxylone*, $C_{16}H_6O(OMe)_4(OH)_2$, a colourless, crystalline substance which corresponds in all its reactions with trimethylbrazilone (this vol., p. 1041), and for which the author therefore proposes the analogous formula



Tetramethylhæmatoxylone.

At the same time, some of the tetramethylhæmatoxylin is further acted on and the product of the reaction contains considerable quantities of 2-carboxy-5 : 6-dimethoxyphenoxyacetic acid and *m*-hemipinic acid,



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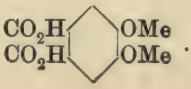


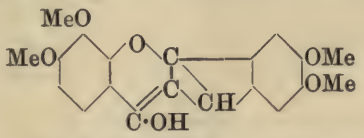
When tetramethylhæmatoxylone is digested with acetic anhydride and anhydrous sodium acetate, it is quantitatively converted into *acetylanhydrotetramethylhæmatoxylone* (m. p. 194°):

$$C_{16}H_6O(OMe)_4(OH)_2 + (CH_3\cdot CO)_2O = C_{16}H_5O(OMe)_4\cdot O\cdot C_2H_3O + H_2O + CH_3\cdot CO_2H,$$

acetylation and elimination of water taking place simultaneously, exactly as in the case of trimethylbrazilone (this vol., p. 1045).

The acetyl compound thus obtained is evidently identical with the tetramethoxymonoacetylhæmatoxylin (compare footnote, this vol., p. 1017) which Herzig (*Monatsh.*, 1895, **16**, 912) first prepared by digesting tetramethyldehydrohæmatoxylin (the author's anhydrotetramethylhæmatoxylone) with sodium acetate and acetic anhydride.

On hydrolysis with methyl alcoholic potash, this acetyl compound is converted, in the first place, into the beautifully crystalline potassium compound of anhydrotetramethylhæmatoxylone, $C_{16}H_5O(OMe)_4\cdot OK$, and this, when decomposed by acids, yields the free anhydro-compound (m. p. 208—210°), which, in the opinion of the author, may be represented by the formula



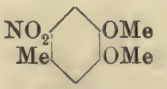
Anhydrotetramethylhæmatoxylone.

The analogy between these derivatives of hæmatoxylin and those of brazilin is complete, since when treated with nitric acid in the cold, tetramethylhæmatoxylone is almost quantitatively converted into *nitrohydroxydihydrotetramethylhæmatoxylone* (m. p. 205°, see p. 1063),

$$C_{16}H_6O(OMe)_4(OH)_2 + HNO_3 = NO_2\cdot C_{16}H_8O_3(OMe)_4\cdot OH,$$

the reaction being exactly similar to that which occurs in the case of the action of nitric acid on trimethylbrazilone.

The hæmatoxylin derivative also dissolves in caustic alkalis with a purple colour and the solution, on standing, becomes brown and deposits a drab precipitate which consists of two substances melting at 118° and 205° respectively. The investigation of these showed that they were identical with the two substances of the same melting points, produced in the same way from nitrohydroxydihydrotrimethylbrazilone by the action of alkalis (this vol., p. 1050), and for which the following formulæ have been proposed:



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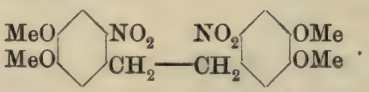
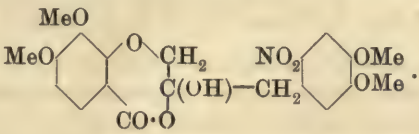


M. p. 118°.

Still more remarkable, perhaps, is the fact that phenylhydrazine converts nitrohydroxydihydrotetramethylhæmatoxylone into the same substance, $C_{24}H_{25}O_4N_5$, as is obtained by the action of phenylhydrazine on the corresponding brazilin derivative (this vol., p. 1053). Obviously, then, the above two reactions are confined, in both cases, to the catechol nuclei in brazilin and hæmatoxylin, and the author therefore suggests, as an expression possibly representing the constitution of *nitrohydroxydihydrotetramethylhæmatoxylone*, the formula



Experimental.

Preparation of Tetramethylhæmatoxylin, $C_{16}H_{10}O_2(OMe)_4$.

In a paper which appeared lately (*Ber.*, 1902, **35**, 1669), and to which reference has already been made, Kostanecki and Lampe give a very convenient method for preparing trimethylbrazilin, namely, by treating the solution of brazilin in alcoholic potash with methyl sulphate instead of with methyl iodide. This modification may also be employed with great advantage in the preparation of tetramethylhæmatoxylin.

Hæmatoxylin, dried at 100° (10 grams), is dissolved in hot methyl alcohol, mixed, while still warm, with methyl alcoholic potash (containing 10 grams of KOH), and then 25 grams of methyl sulphate are added all at once. As soon as the reaction is over, a second addition of the same quantities of methyl alcoholic potash and methyl sulphate is made and the product is then cooled and mixed with four times its volume of water. The clear solution gradually deposits needle-shaped crystals, and after two days these are collected, washed with water, and allowed to dry at the ordinary temperature on porous plates; the yield is about 8 grams.

The tetramethylhæmatoxylin so obtained is almost always in the hydrated form, the crystals apparently having the composition $C_{20}H_{22}O_6,2H_2O$. After recrystallisation from dilute methyl alcohol, it was obtained in long, glistening, colourless needles which melted at about 65—68° and on analysis gave the following results:

0·1595 gave 0·3586 CO_2 and 0·0946 H_2O. C = 61·2; H = 6·6.

$C_{20}H_{22}O_6,2H_2O$ requires C = 60·9; H = 6·6 per cent.

The determination of the water of crystallisation gave the following results:

0·3785, on slowly heating to 110°, lost 0·0413 H_2O. $H_2O = 10·0$.
$C_{20}H_{22}O_6,2H_2O$ requires $H_2O = 9·2$ per cent.

The residue, which is somewhat discoloured, gives, on recrystallisation from dilute alcohol, sometimes the hydrated crystals and sometimes anhydrous tetramethylhæmatoxylin melting at 142°, but frequently the two forms separate out side by side.

Tetramethylhæmatoxylone, $C_{16}H_6O(OMe)_4(OH)_2$.

This substance, which is formed by the action of chromic acid on tetramethylhæmatoxylin, was first prepared as follows.

Tetramethylhæmatoxylin (5 grams) was ground to a fine paste with water, mixed with 400 c.c. of potassium dichromate solution (containing 40 grams in the litre) and 120 grams of 30 per cent. sulphuric acid, and heated in a water-bath at 35—40° for about two hours. The precipitate was collected on the pump, and after drying on a porous plate, digested with benzene which extracted the tetramethylhæmatoxylone, but left a violet, amorphous substance undissolved. The benzene solution was then evaporated to a small bulk and mixed with alcohol and the crude tetramethylhæmatoxylone, which separated on standing, purified by recrystallisation from much alcohol. On analysis:

0·1852 gave 0·4355 CO_2 and 0·0907 H_2O. $C = 64·2$; $H = 5·4$.
$C_{20}H_{20}O_7$ requires $C = 64·5$; $H = 5·3$ per cent.

As the yield obtained by this process is only about 30 per cent. of the theoretical, experiments were made on the oxidation by chromic acid under different conditions, when it was found that the following process, which is similar to that used in the preparation of trimethylbrazilone (this vol., p. 1041), gives excellent results.

Tetramethylhæmatoxylin (10 grams) is dissolved in 50 grams of warm glacial acetic acid, and, after cooling, a solution of 6 grams of chromic acid in a little water is added in small quantities at a time, care being taken that the temperature does not rise above 30°. The precipitate which separates on standing is collected on the pump and washed with glacial acetic acid, when a pale yellow, crystalline mass is obtained which melts at 190—195° with rapid evolution of gas, and consists of nearly pure tetramethylhæmatoxylone, the yield being about 8 grams. After recrystallisation from much alcohol, it gave, on analysis, the following numbers:

0·1665 gave 0·3933 CO_2 and 0·0816 H_2O. $C = 64·4$; $H = 5·4$.
$C_{20}H_{20}O_7$ requires $C = 64·5$; $H = 5·3$ per cent.

Prepared by either of the above processes, tetramethylhæmatoxylone

is obtained always as a straw-coloured, crystalline mass, but it is, in reality, quite colourless (see p. 1065). It is sparingly soluble in alcohol, acetone, and most other solvents, with the exception of toluene and acetic acid, and from the latter it can be readily crystallised. It dissolves in concentrated sulphuric acid with an orange-red colour. The methoxy-groups were determined by Zeisel's method with the following results:

0·3842 gave 0·9774 AgI. MeO = 33·5.

$C_{16}H_8O_3(OMe)_4$ requires MeO = 33·3 per cent.

Examination of the Chromium Liquors from the Oxidation of Tetramethylhæmatoxylin.

The aqueous liquors which had accumulated in the preparation of considerable quantities of tetramethylhæmatoxylone by the first method given on p. 1060 were repeatedly extracted with ether; the ethereal solution was dried over calcium chloride, when a dark brown oil was obtained which, on standing, became semi-solid. This was boiled with a considerable bulk of water, when nearly all dissolved, and after decolorising with animal charcoal and evaporating to a small bulk, the solution deposited brown, prismatic crystals which are almost insoluble in water. The crystals were collected and recrystallised from glacial acetic acid, and thus obtained in colourless needles melting at 214—216° and decomposing at about 220—230°. On analysis:

0·1271 gave 0·2405 CO_2 and 0·0541 H_2O. C = 51·6; H = 4·7.
0·1442 „ 0·2721 CO_2 „ 0·0624 H_2O. C = 51·4; H = 4·8.

$C_{11}H_{12}O_7$ requires C = 51·5; H = 4·7 per cent.

The *silver* salt, $C_{11}H_{10}O_7Ag_2$, was obtained on adding silver nitrate to the neutral solution of the ammonium salt as a white, gelatinous precipitate which gave the following results on analysis:

0·2305 gave 0·2365 CO_2, 0·045 H_2O, and 0·1055 Ag. C = 28·0; H = 2·2; Ag = 45·8.

$C_{11}H_{10}O_7Ag_2$ requires C = 28·1; H = 2·1; Ag = 45·9 per cent.

There can be no doubt that this dibasic acid is 2-carboxy-5:6-dimethoxyphenoxyacetic acid and identical with the acid of the same melting point which was obtained by the oxidation of tetramethylhæmatoxylin with potassium permanganate as described in a previous paper (Trans., 1902, 81, 241).

The aqueous solution, from which the above acid had crystallised, deposited, on evaporation over sulphuric acid in a vacuum desiccator, large, glistening, brown prisms which became opaque at 100° and

melted at 187—190° with vigorous decomposition and showed all the properties of *m*-hemipinic acid. On analysis:

0·1291 gave 0·2502 CO_2 and 0·0526 H_2O. C = 52·9; H = 4·5.
$C_{10}H_{10}O_6$ requires C = 53·1; H = 4·4 per cent.

This acid was further identified by conversion into the characteristic ethylimide which, after recrystallisation from alcohol, melted at 228—230°. The mother liquors from this *m*-hemipinic acid contained considerable quantities of oxalic acid.

Acetylanhydrotetramethylhæmatoxylone, $C_{16}H_5O(OMe)_4 \cdot O \cdot C_2H_3O$.

In preparing this substance, tetramethylhæmatoxylone (8 grams) was mixed with 5 grams of anhydrous sodium acetate and 40 grams of acetic anhydride and the whole heated to boiling in a reflux apparatus for about 15 minutes. The clear liquid, after cooling, was poured into much ice-water and well shaken until the excess of acetic anhydride had been decomposed, the precipitate was then collected on the pump and washed with water. It was then dissolved in hot glacial acetic acid containing 10 per cent. of acetic anhydride, when, on cooling, large, colourless, glistening prisms separated which melted at 193—194° and gave on analysis the following results:

0·1501 gave 0·3664 CO_2 and 0·0678 H_2O. C = 66·5; H = 5·1.
$C_{22}H_{20}O_7$ requires C = 66·7; H = 5·0 per cent.

This substance is evidently identical with the tetramethoxymonoacetylhæmatoxylin * (m. p. 190—192°) which Herzig (*Monatsh.*, 1895, 16, 912) obtained by digesting tetramethyldehydrohæmatoxylin with sodium acetate and acetic anhydride. Herzig states that solutions of the pure substance possess a distinct blue fluorescence, and this was also noticed in the case of the preparation described above before it was recrystallised. But after twice crystallising the substance the fluorescence had entirely disappeared, and it is therefore evidently due to minute traces of some impurity.

Anhydrotetramethylhæmatoxylone, $C_{16}H_5O(OMe)_4 \cdot OH$.

When finely powdered acetylanhydrotetramethylhæmatoxylone (2 grams), was boiled with dilute methyl alcoholic potash (containing 2 grams of hydroxide), it rapidly dissolved, and if the solution was filtered and allowed to stand overnight, a mass of colourless, glistening crystals of the *potassium* compound of anhydrotetramethylhæmatoxylone

* The reason for altering these names in the present paper is given in the footnote on p. 1017.

separated. This was collected on the pump, washed well with methyl alcohol, and dried at 100°, when the crystals became opaque and gradually broke up into a fine powder, which, on analysis, gave the following results:

0·4527 gave 0·0981 K_2SO_4. K = 9·7.

$C_{20}H_{17}O_6K$ requires K = 10·0 per cent.

On standing in the air, this potassium compound gradually acquires a pale green colour; it is soluble in water to some extent, but is mostly decomposed on mixing with water, the liquid becoming strongly alkaline. It is easily decomposed by dilute acetic acid, yielding a sticky precipitate which rapidly hardens and becomes crystalline and then consists of nearly pure anhydrotetramethylhæmatoxylone. This was collected, washed with water, and crystallised from boiling alcohol, from which it separates in small, glistening prisms. On analysis:

0·1452 gave 0·3626 CO_2 and 0·0713 H_2O. C = 68·1; H = 5·4.
0·1599 „ 0·3972 CO_2 „ 0·0765 H_2O. C = 67·7; H = 5·3.

$C_{20}H_{18}O_6$ requires C = 67·8; H = 5·1 per cent.

Anhydrotetramethylhæmatoxylone melts at 208—210° and is sparingly soluble in benzene, toluene, or cold alcohol, but dissolves fairly easily in the latter on boiling; it is also soluble in boiling acetic acid, more readily in hot chloroform, and still more readily in boiling acetone; it dissolves in concentrated sulphuric acid with an orange colour. The addition of bromine to the solution in chloroform causes the separation of a brown precipitate, hydrogen bromide being given off at the same time. When carefully heated in a current of nitrogen, the anhydro-compound yields a small quantity of a yellow sublimate, then the substance decomposes and a quantity of oil distils leaving a considerable carbonaceous residue.

Anhydrotetramethylhæmatoxylone was first prepared by Herzig (*Monatsh.*, 1895, **16**, 910) by oxidising acetylmethylhæmatoxylin with chromic acid in acetic acid solution; he named it tetramethyldehydrohæmatoxylin and gave the melting point at 202—206°. Herzig states that he could not obtain the substance quite pure on account of its tendency to change in the air, but the substance prepared by the method described above seemed to be perfectly stable, no change being noticeable even after standing for some days exposed to the air.

Nitrohydroxydihydrotetramethylhæmatoxylone,
$NO_2 \cdot C_{16}H_8O_3(OMe)_4 \cdot OH$.

This substance was first prepared by the action of *dilute* nitric acid on tetramethylhæmatoxylone, which was ground to a fine paste with water and then heated with dilute nitric acid (sp. gr. 1·25)

for 7—8 hours at 40—45°. After allowing the mixture to stand overnight, the precipitate was collected, washed with water, drained on a porous plate, and crystallised from glacial acetic acid. The pale yellow, needle-shaped crystals thus obtained were found to contain some unchanged tetramethylhæmatoxylone. The mass was therefore repeatedly treated with boiling toluene, which extracts the latter, but in which the nitro-compound is practically insoluble. Finally, the substance was again crystallised from acetic acid and analysed:

0·1556 gave 0·3145 CO_2 and 0·0724 H_2O. C = 55·1; H = 5·1.
0·1567 „ 4·6 c.c. nitrogen at 18° and 750 mm. N = 3·3.
$C_{20}H_{21}O_{10}N$ requires C = 55·2; H = 4·9; N = 3·2 per cent.

As in the case of the corresponding nitro-compound from trimethylbrazilone, the method just described gives the purer product, but in preparing large quantities of nitrohydroxydihydrotetramethylhæmatoxylone the following process is much more convenient.

Finely powdered tetramethylhæmatoxylone (5 grams) is gradually added to colourless, concentrated nitric acid (30 c.c.), in which it dissolves completely, care being taken to avoid any rise of temperature above 25°. After standing for 5 minutes, the brownish-yellow liquid is poured into water, the ochreous precipitate collected, washed with water, and purified by crystallisation exactly as described above, but as a rule the product (which is obtained in a yield of 80—85 per cent.) will be found to contain very little unchanged tetramethylhæmatoxylone. The nitro-compound prepared in this way was always much more deeply coloured than that obtained by the process first described; it, however, gave correct numbers on analysis:

0·1871 gave 0·3803 CO_2 and 0·0854 H_2O. C = 55·4; H = 5·1.
0·1585 „ 4·7 c.c. nitrogen at 16° and 757 mm. N = 3·4.
$C_{20}H_{21}O_{10}N$ requires C = 55·2; H = 4·9; N = 3·2 per cent.

Nitrohydroxydihydrotetramethylhæmatoxylone melts at 204—205° with darkening and evolution of gas, and is sparingly soluble in alcohol, benzene, toluene, or most other organic solvents, even on boiling, but it dissolves readily in boiling glacial acetic acid, and separates on cooling almost completely in pale sulphur-yellow needles.

It is insoluble in dilute sodium carbonate, but dissolves readily and completely in caustic soda, forming an intense violet solution which, on standing, loses its colour and deposits a drab precipitate, exactly as in the case of the corresponding nitrohydroxydihydrotrimethylbrazilone (this vol., p. 1050).

The nitric acid mother liquors from the preparation of nitrohydroxydihydrotetramethylhæmatoxylin were saturated with ammonium sulph-

ate and extracted repeatedly with ether. The ethereal solution was concentrated on the water-bath and afterwards allowed to evaporate to dryness in an open dish at the ordinary temperature.

The deep yellow residue was left in contact with porous porcelain until quite dry and then recrystallised several times from glacial acetic acid. In this way, a considerable quantity of a colourless acid was obtained which melted at 215°, and on examination was found to consist of 2-carboxy-5 : 6-dimethoxyphenoxyacetic acid, identical with the acid already obtained by oxidising tetramethylhæmatoxylin with permanganate (this vol., p. 241). On analysis :

0·1039 gave 0·1959 CO_2 and 0 0452 H_2O. C = 51·5 ; H = 4·8.
$C_{11}H_{12}O_7$ requires C = 51·6 ; H = 4·7 per cent.

The toluene liquors from the purification of a large quantity of nitrohydroxydihydrotetramethylhæmatoxylone in the way described above, yielded, on concentration, crystals which separated from acetic acid in *perfectly colourless*, glistening needles of melting point 195°. That this substance was pure tetramethylhæmatoxylone was shown by the following analysis :

0·1457 gave 0·3442 CO_2 and 0·0708 H_2O. C = 64·4 ; H = 5·4.
$C_{20}H_{20}O_7$ requires C = 64·5 ; H = 5·3 per cent.

Action of Potash on Nitrohydroxydihydrotetramethylhæmatoxylone.

This decomposition proceeds on very similar lines to that described in the case of the nitro-compound from brazilin. The nitro-compound employed in the present experiments was that directly obtained by adding water to the product of the action of nitric acid on tetramethylhæmatoxylone. This was treated with potash in exactly the same way as described on p. 1050, and when the purple colour had disappeared the drab precipitate was collected, washed with water, and treated with boiling alcohol.

By this means, the product was separated into two substances which melted at 205° and 118° respectively, and which were found to be identical with those obtained from brazilin.

The substance of melting point 205° gave the following result on analysis :

0·1721 gave 10·5 c.c. nitrogen at 15° and 762 mm. N = 7·2.

The determination of the nitrogen in the substance of melting point 118° gave :

0·1742 gave 10·6 c.c. nitrogen at 16° and 766 mm. N = 7·2.
$C_9H_{11}O_4N$ requires N = 7·1 per cent.

The alkaline aqueous solution from the drab precipitate was very dark coloured, and, as in the case of the corresponding brazilin decom position, gave on acidifying a nearly black, resinous mass. This has not yet been further investigated.

Action of Phenylhydrazine on Nitrohydroxydihydrotrimethylhæmatoxylone.—In studying this action, the pure nitro-compound (2 grams) was dissolved in hot glacial acetic acid (20 grams), and when the temperature had fallen to about 40°, 4 grams of pure phenylhydrazine were added. The liquid soon began to deposit orange crystals, and on the following day these were collected on the pump, washed well with acetic acid, dried at 100°, and analysed:

0·1365 gave 0·0709 H_2O and 0·3208 H_2O. C = 64·4; H = 5·8.
0·1707 „ 24 c.c. nitrogen at 23° and 766 mm. N = 15·9.
$C_{24}H_{25}O_4N_5$ requires C = 64·4; H = 5·6; N = 15·7 per cent.

This substance melts at 170°, and a careful comparison showed that it is identical with the compound obtained by the action of phenylhydrazine on nitrohydroxydihydrotrimethylbrazilone (this vol., p. 1053).

As in this latter case, the dark coloured mother liquors from the orange crystals gave, on the addition of water, an ochreous precipitate, which, however, has not yet been investigated.

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DEUTSCHEN CHEMISCHEN GESELLSCHAFT.

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342. W. H. Perkin jun.: Die synthetische Darstellung von Kohlenstoffringen.

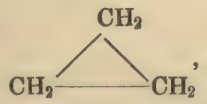
BERLIN 1902.

342. W. H. Perkin jun.: Die synthetische Darstellung von Kohlenstoffringen.

(Vortrag, gehalten vor der Deutschen chemischen Gesellschaft am 3. Mai 1902.)

Zu allererst möchte ich dem geehrten Vorstande der Deutschen chemischen Gesellschaft meinen verbindlichen Dank dafür aussprechen, dass er mich mit der Einladung geehrt und erfreut hat, Ihnen hier einen Vortrag zu halten; ich hoffe, dass es mir gelingen wird, Ihnen das Thema der synthetischen Bildungen von geschlossenen Kohlenstoffketten einigermaassen interessant zu machen.

Das Studium der geschlossenen Kohlenstoffketten beschäftigt die Chemiker schon lange, und es schien eine scharfe Grenze gezogen zwischen den Verbindungen der offenen Kohlenstoffketten und den »aromatischen« oder Benzol-Verbindungen. Dazu trug schon der Umstand bei, dass in der Natur zwischen den Ersteren, z. B. den Zuckerarten, und den Benzolverbindungen, z. B. den ätherischen Oelen, kein Uebergang zu bestehen schien, sowie die Thatsache, dass Versuche zur synthetischen Darstellung von cyclischen Verbindungen mit weniger als sechs Kohlenstoffatomen gescheitert waren. So gab Reboul[1]) an, dass Trimethylen,



durch Einwirkung von metallischem Natrium auf Trimethylendibromid,

$$CH_2Br.CH_2.CH_2Br.,$$

nicht erhältlich sei.

[1]) Reboul, A. ch. [5] 14, 448.

Diese inzwischen als unrichtig erwiesene Angabe, sowie ähnliche negative Resultate führten Victor Meyer[1]) im Jahre 1875 zur Behauptung, dass die Existenz eines Dreikohlenstoffringes sehr unwahrscheinlich wäre.

Nunmehr jedoch ist es bekannte Thatsache, dass nicht nur der Dreikohlenstoffring, sondern auch Ringe mit 4, 5, 7 und 8 Kohlenstoffatomen synthetisch dargestellt werden können, und die scharfe Grenze zwischen den Verbindungen mit offener Kohlenstoffkette und denen, welche einen aus sechs Kohlenstoffatomen bestehenden Ring enthalten, ist aus dem Felde geräumt.

Die vereinten Bemühungen der zahlreichen Chemiker, welche es sich während der letzten zwanzig Jahre zur Aufgabe gestellt haben, das Problem der Ringbildung experimentell zu erforschen, haben der organischen Chemie ein neues weites Gebiet eröffnet, ein Gebiet, auf dem viel geleistet wurde, das jedoch noch immer nur sehr unvollkommen erforscht ist.

In dasselbe gehören auch die Terpene und Campherarten; und was die letzten 15 Jahre in der Erkenntniss der chemischen Beschaffenheit dieser so wichtigen Naturproducte gebracht haben, ist in erster Linie den Untersuchungen über die einfachen Ringverbindungen zu verdanken.

Es dürfte angezeigt sein, dem Gegenstande des Vortrages eine Zusammenfassung der bis heute bekannten synthetischen Darstellungsmethoden der Ringverbindungen vorauszuschicken:

I. Die einfachste Methode zur Bildung cyclischer Kohlenwasserstoffe besteht in der Einwirkung von Natrium, Zink oder anderen geeigneten Metallen auf die Dibromsubstitutionsproducte aliphatischer Kohlenwasserstoffe.

So gelang es Freund[2]), im Widerspruch zu Reboul[3]), aus Trimethylendibromid mittels Natrium (oder besser mittels Zink) das Trimethylen darzustellen:

$$CH_2<\begin{matrix}CH_2Br\\CH_2Br\end{matrix} + 2Na = CH_2<\begin{matrix}CH_2\\CH_2\end{matrix} + 2NaBr,$$

und später wurde aus Hexamethylendibromid durch Erwärmen mit metallischem Natrium (in Xylollösung) das Hexamethylen[4]) erhalten:

$$CH_2<\begin{matrix}CH_2-CH_2\\CH_2.CH_2Br\end{matrix}>CH_2Br \longrightarrow CH_2<\begin{matrix}CH_2.CH_2\\CH_2.CH_2\end{matrix}>CH_2.$$

Dieselbe Synthese fand zur Darstellung vieler anderer Ring-Kohlenwasserstoffe Verwendung.

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[1]) V. Meyer, Ann. d. Chem. 180, 196.
[2]) Freund, M. 3, 626. [3]) Reboul, A. ch. [5] 14, 488.
[4]) Haworth, Perkin, Soc. 65, 599.

II. Cyclische Carbonsäuren lassen sich synthetisch mit Hülfe von Malonester darstellen. Die Natriumverbindung des Esters wird mit Aethylendibromid, Trimethylendibromid oder ähnlichen aliphatischen Dibromiden behandelt[1]):

$$\begin{matrix}CH_2Br\\ \dot{C}H_2Br\end{matrix} + Na_2C(CO_2C_2H_5)_2 = \begin{matrix}CH_2\\ \dot{C}H_2\end{matrix}\!>\!C(CO_2C_2H_5)_2 + 2NaBr$$

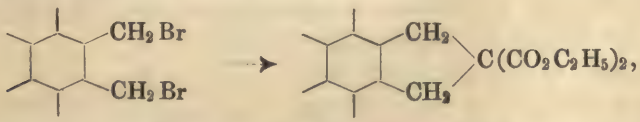
$$CH_2\!<\!\begin{matrix}CH_2Br\\ CH_2Br\end{matrix} \text{ ergiebt } CH_2\!<\!\begin{matrix}CH_2\\ CH_2\end{matrix}\!>\!C(CO_2C_2H_5)_2$$

$$\begin{matrix}CH_2.CH_2.CH_2Br\\ \dot{C}H_2.CH_2Br\end{matrix} \text{ ergiebt } \begin{matrix}CH_2.CH_2.CH_2\\ \dot{C}H_2.CH_2.\dot{C}(CO_2C_2H_5)_2\end{matrix}.$$

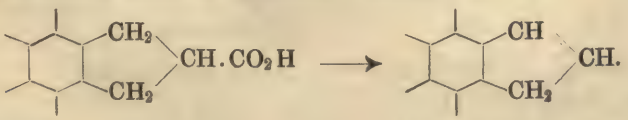
Die so erhaltenen Ester werden durch Hydrolyse in die entsprechenden Dicarbonsäuren übergeführt, welche bei der Destillation unter Entwickelung von Kohlensäure in die Monocarbonsäuren übergehen:

$CH_2\!<\!\begin{matrix}CH_2\\ CH.CO_2H\end{matrix}$	$\begin{matrix}CH_2.CH_2\\ CH_2.CH.CO_2H\end{matrix}$	$\begin{matrix}CH_2.CH_2.CH_2\\ CH_2.CH_2.CH.CO_2H\end{matrix}$.
Trimethylen-carbonsäure	Tetramethylen-carbonsäure	Hexamethylen-carbonsäure.

Diese synthetische Methode ermöglichte auch die Darstellung von cyclischen Verbindungen, welche ausserdem den Benzolring[2]) enthalten. So wurde durch Einwirkung von *o*-Xylylendibromid auf Malonester Hydrindendicarbonsäureester erhalten:



der nachher durch Hydrolyse und Kohlensäureabspaltung in Hydrindencarbonsäure übergeführt wurde. Das Baryumsalz der Letzteren ergab bei der Destillation den Kohlenwasserstoff Inden, der sich mit dem Kohlenwasserstoff identisch erwies, welcher von Krämer und Spilker[3]) aus Steinkohlentheer gewonnen wurde:

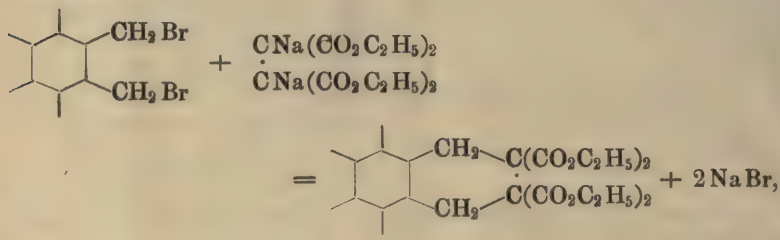


[1]) Perkin, diese Berichte 17, 54 [1884]; Fittig, Röder, Ann. d. Chem. 227, 13.

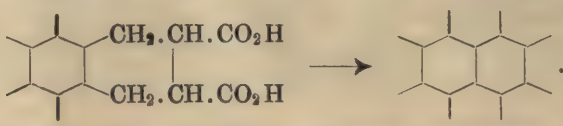
[2]) Baeyer, Perkin, diese Berichte 17, 125 [1884]; Perkin, Révay, Soc. 65, 228.

[3]) Krämer, Spilker, diese Berichte 23, 3276 [1890].

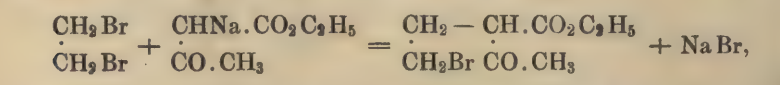
Es gelang ferner, durch eine Modification dieser Methode auf synthetischem Wege Abkömmlinge des Tetrahydronaphtalins[1]) und das Naphtalin selbst zu erhalten. Es wurde *o*-Xylylendibromid auf das Dinatriumsubstitutionsproduct von Aethantetracarbonester zur Einwirkung gebracht:



und der dadurch erhaltene Ester durch Kochen mit Kali unter Abspaltung von Kohlensäure in Tetrahydronaphtalindicarbonsäure übergeführt, deren Silbersalz bei der Destillation Naphtalin ergab:

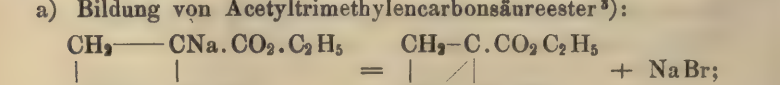


Wenn bei diesen Synthesen der Malonester durch Acetessigester, Benzoylessigester oder Acetondicarbonsäureester ersetzt wird, vollzieht sich die Reaction nicht immer in der gleichen Weise. Wird z. B. Aethylendibromid mit Natriumacetessigester behandelt, so erfolgt zunächst die Bildung von Bromäthylacetessigester[2]):

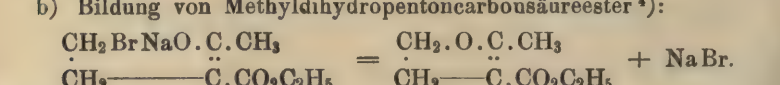


der bei weiterer Behandlung mit Natriumäthylat den folgenden beiden Ringbildungen unterliegt:

a) Bildung von Acetyltrimethylencarbonsäureester[3]):



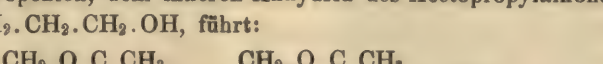
b) Bildung von Methyldihydropentoncarbonsäureester[4]):



[1]) Baeyer, Perkin, diese Berichte 17, 448 [1884]; Perkin, Soc. 53, 1.
[2]) Perkin, Freer, Soc. 51, 833.
[3]) Perkin, Soc. 47, 850. [4]) Marshall und Perkin, Soc. 59, 878.

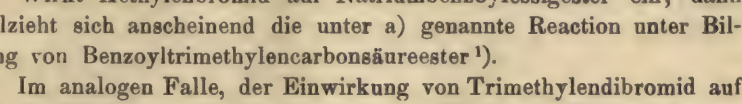
Acetyltrimethylencarbonsäureester ergiebt durch Hydrolyse die freie Säure, welche durch Destillation unter Kohlensäureabspaltung in Acetyltrimethylen übergeht:

während Methyldihydropentoncarbonsäureester in gleicher Weise zum Methyldihydropenton, dem inneren Anhydrid des Acetopropylalkohols, $CH_3.CO.CH_2.CH_2.CH_2.OH$, führt:

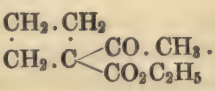


Wirkt Aethylenbromid auf Natriumbenzoylessigester ein, dann vollzieht sich anscheinend die unter a) genannte Reaction unter Bildung von Benzoyltrimethylencarbonsäureester [1]).

Im analogen Falle, der Einwirkung von Trimethylendibromid auf Natriumacetessigester, wickelt sich nur der eine Process ab unter Bildung von Methyldihydrohexoncarbonsäureester [2]):

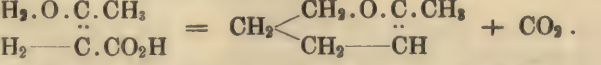


und es entstehen auch nicht einmal Spuren von Acetyltetramethylencarbonsäureester:



In gleicher Weise geht die Reaction unter Verwendung von Benzoylessigester vor sich, wobei Phenyldihydrohexoncarbonsäureester entsteht.

Der Methyldihydrohexoncarbonsäureester ist eine interessante Substanz, weil er durch Hydrolyse in die entsprechende Säure übergeht und diese dann durch Destillation unter Kohlensäureabspaltung Methyldihydrohexon bildet — das innere Anhydrid des Acetylbutylalkohols, $CH_3.CO.CH_2.CH_2.CH_2.CH_2.OH$:



III. Eine weitere Methode, welche sich zur synthetischen Darstellung von Carbonsäuren mit geschlossener Kohlenstoffkette als sehr werthvoll erwies, ist in folgenden Beispielen erläutert:

---

[1]) Perkin, Soc. 47, 840; Freer und Perkin, Soc. 51, 837

[2]) Perkin, Soc. 51, 709.

a) Wird Aethylenchlorid in alkoholischer Lösung mit Natriummalonester behandelt, so vollzieht sich zum Theil die folgende Umsetzung[1]):

$$\begin{matrix}CH_2Cl\\CH_2Cl\end{matrix} + \begin{matrix}NaCH(CO_2C_2H_5)_2\\NaCH(CO_2C_2H_5)_2\end{matrix} = \begin{matrix}CH_2.CH(CO_2C_2H_5)_2\\CH_2.CH(CO_2C_2H_5)_2\end{matrix} + 2\,NaCl.$$

Wird der so erhaltene Butantetracarbonsäureester in die Dinatriumverbindung übergeführt und diese sodann mit Jod oder Brom behandelt, so vollzieht sich eine Ringschliessung unter Bildung von Tetramethylentetracarbonsäureester:

$$\begin{matrix}CH_2.CNa(CO_2C_2H_5)_2\\CH_2.CNa(CO_2C_2H_5)_2\end{matrix} + Br_2 = \begin{matrix}CH_2.C(CO_2C_2H_5)_2\\CH_2.C(CO_2C_2H_5)_2\end{matrix} + 2\,NaBr.$$

b) Aehnlich resultiren aus Trimethylendibromid der Pentantetracarbonsäureester und Pentamethylentetracarbonsäureester[2]):

$$CH_2\!<\!\begin{matrix}CH_2.CH(CO_2C_2H_5)_2\\CH_2.CH(CO_2C_2H_5)_2\end{matrix} \text{ und } CH_2\!<\!\begin{matrix}CH_2.C(CO_2C_2H_5)_2\\CH_2.C(CO_2C_2H_5)_2\end{matrix}.$$

Die unter a) und b) erhaltenen Ester gehen durch Hydrolyse und Kohlensäureabspaltung in Tetramethylen-1.2-dicarbonsäure und Pentamethylen-1.2-dicarbonsäure über:

$$\begin{matrix}CH_2.CH.CO_2H\\CH_2.CH.CO_2H\end{matrix} \text{ und } CH_2\!<\!\begin{matrix}CH_2.CH.CO_2H\\CH_2.CH.CO_2H\end{matrix},$$

welche beide in wohlcharakterisirten *cis*- und *trans*-Modificationen existiren.

Pentantetracarbonsäureester wurde auch für andere Synthesen vortheilhaft verwerthet. Seine Dinatriumverbindung setzt sich nämlich mit Methylenjodid zum Hexamethylentetracarbonsäureester[3]) um:

$$CH_2\!<\!\begin{matrix}CH_2.CNa(CO_2C_2H_5)_2\\CH_2.CNa(CO_2C_2H_5)_2\end{matrix} + CH_2J_2 = CH_2\!<\!\begin{matrix}CH_2.C(CO_2C_2H_5)_2\\\quad\quad>CH_2\\CH_2.C(CO_2C_2H_5)_2\end{matrix} + 2\,NaJ.$$

Derselbe erwies sich als besonders interessant, weil er durch Hydrolyse und Kohlensäureabspaltung in die *cis*- und *trans*-Modificationen von Hexahydroisophtalsäure verwandelt werden konnte,

$$CH_2\!<\!\begin{matrix}CH_2.CH.CO_2H\\\quad\quad>CH_2\\CH_2.CH.CO_2H\end{matrix},$$

in die Säuren nämlich, die bald nachher von Baeyer und Villiger[4]) durch Reduction von Isophtalsäure gewonnen wurden.

IV. Eine Methode zur Darstellung cyclischer Glykole beruht auf der Beobachtung, dass durch Reduction gewisser Diketone mit

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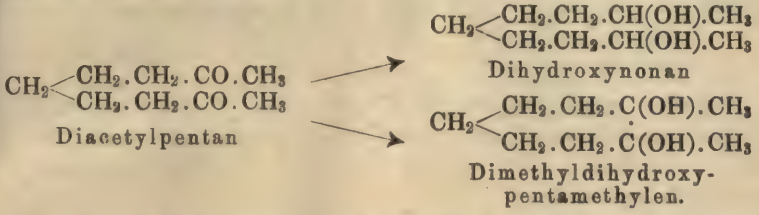
[1]) Perkin, Soc. 65, 578. [2]) Perkin, Soc. 51, 241.
[3]) Perkin, Soc. 59, 798.
[4]) Baeyer und Villiger, Ann. d. Chem. 276, 259.

Natrium und wasserhaltigem Aether Reaction in zweierlei Richtung stattfindet, und zwar einerseits unter Bildung des Glykols mit offener Kohlenstoffkette, andererseits — durch intramolekulare Pinakoncondensation — unter Bildung eines Glykols, welches einen Kohlenstoffring enthält[1]), z. B.:



Diese Synthese ist nicht häufig benutzt worden, weil es schwer ist, zu den nöthigen Diketonen zu gelangen, hauptsächlich aber wegen der schwierigen Trennung der beiden Glykole.

Kurz nach Auffindung dieser Methode hat J. Wislicenus[2]) eine Reihe interessanter Arbeiten über den Gegenstand veröffentlicht, in denen er zeigte, dass bei der Reduction von α,γ-Dibenzoylpropan 1.2-Diphenyldihydroxypentamethylen entsteht:

$$CH_2\begin{<}CH_2.CO\,C_6H_5\\CH_2.CO\,C_6H_5\end{} + 2H = CH_2\begin{<}CH_2.C(OH).C_6H_5\\CH_2.C(OH).C_6H_5\end{}.$$

Diese Reaction ist aber als eine sehr verwickelte zu betrachten, da Japp und Michie[3]) nachher fanden, dass das Reactionsproduct nicht weniger als fünf schwer isolirbare Verbindungen enthielt, deren eine als Diphenyldihydroxypentamethylen angesprochen werden kann.

V. Ketonderivate von ungesättigten Ringen sind aus gewissen Diketonen durch Einwirkung wasserentziehender Agentien erhältlich, z. B. durch Schwefelsäure, wobei eine Reaction eintritt, ähnlich der bei der Bildung von Mesityloxyd aus zwei Molekülen Aceton.

Derart geht Diacetylbutan durch Auflösung in concentrirter Schwefelsäure in Methyldihydrocyclopentenmethylketon[4]) über:

$$CH_2\begin{<}CH_2.CH_2.CO.CH_3\\CH_2.CO.CH_3\end{} = CH_2\begin{<}CH_2.\dot{C}.CO.CH_3\\CH_2.\dot{C}.CH_3\end{} + H_2O,$$

während Diacetylpentan unter ähnlichen Verhältnissen *o*-Methyltetrahydrobenzolmethylketon[5]) ergiebt:

$$\begin{matrix}CH_2.CH_2.CH_2.CO.CH_3\\CH_2.CH_2.CO.CH_3\end{matrix} = \begin{matrix}CH_2.CH_2.\dot{C}.CO.CH_3\\CH_2.CH_2.\dot{C}.CH_3\end{matrix} + H_2O.$$

[1]) Kipping und Perkin, Soc. 59, 214.
[2]) Wislicenus, Ann. d. Chem. 302, 194.
[3]) Japp und Michie, Soc. 79, 1011.
[4]) Marshall und Perkin, Soc. 57, 241.
[5]) Kipping und Perkin, Soc. 57, 14.

Drei Jahre nach Veröffentlichung dieser Arbeiten hat Hagemann[1]) einige interessante Untersuchungen in gleicher Richtung angestellt. Er versuchte die Darstellung von Diacetylpropan,

$$CH_3.CO.CH_2.CH_2.CH_2.CO.CH_3,$$

fand aber, dass dieselbe wegen der leichten inneren Condensation unmöglich war, und erhielt statt dessen Methylketotetrahydrobenzol.

$$\begin{matrix} CH_2.CH_2.CO.CH_3 \\ CH_2.CO.CH_3 \end{matrix} = \begin{matrix} CH_2.CH_2.C.CH_3 \\ CH_2.CO.CH \end{matrix} + H_2O.$$

Ungefähr gleichzeitig zeigten Knoevenagel[2]) und Neurath[3]), dass Isobutylidenacetessigester durch innere Condensation mit Leichtigkeit einen Ester bildet, welcher durch Hydrolyse Methylisopropyltetrahydrobenzol liefert:

$$\begin{matrix} C_2H_5O_2C.CH.CO.CH_3 \\ CH_3 \\ CH_3 \\ C_2H_5O_2C.CH.CO.CH_3 \end{matrix} > CH.CH \rightarrow \begin{matrix} C_2H_5O_2C.CH.C.CH_3 \\ CH_3 \\ CH_3 \\ C_2H_5O_2C.CH.CO \end{matrix} > CH.CH\ CH \rightarrow \begin{matrix} CH_2.C.CH_3 \\ CH_3 \\ CH_3 \\ CH_2.CO \end{matrix} > CH.CH\ CH .$$

Ebenso verhalten sich viele andere ähnlich constituirte Diketoverbindungen.

VI. Eine andere wichtige Synthese zur Herstellung von Verbindungen mit geschlossener Kohlenstoffkette ist in den letzten Jahren von Dieckmann[4]) bearbeitet worden. Derselbe fand, dass eine, der Herstellung von Acetessigester aus zwei Molekülen Essigester ähnliche Reaction sich erzielen lasse durch Einwirkung von metallischem Natrium auf die Ester gewisser zweibasischer Säuren. So erhielt er aus Adipinsäureester mittels Natrium den Ketopentamethylencarbonsäureester:

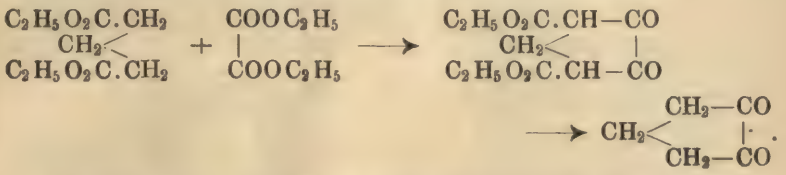
$$\begin{matrix} CH_2 \\ CH_2 \quad CH_2 \\ C_2H_5O.CO \quad CH_2.CO_2C_2H_5 \end{matrix} \rightarrow \begin{matrix} CH_2 \\ CH_2 \quad CH_2 \\ CO-CH.CO_2C_2H_5 \end{matrix},$$

und gleicherweise aus Pimelinsäureester den Ketohexamethylencarbonsäureester:

$$\begin{matrix} CH_2 \\ CH_2 \quad CH_2 \\ C_2H_5O.CO \quad CH_2 \\ \quad\quad CH_2.CO_2C_2H_5 \end{matrix} \rightarrow \begin{matrix} CH_2 \\ CH_2 \quad CH_2 \\ CO \quad CH_2 \\ \quad\quad CH.CO_2C_2H_5 \end{matrix}.$$

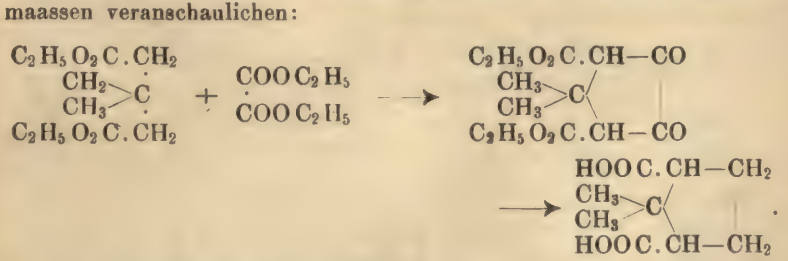
[1]) Hagemann, diese Berichte **26**, 876 [1893].
[2]) Knoevenagel, Ann. d. Chem. **289**, 131 [1896].
[3]) Neurath, Dissertation, Berlin 1895.
[4]) Dieckmann, diese Berichte **27**, 102 [1894].

Dieckmann[1]) veröffentlichte bald nachher eine Abänderung dieser Synthese, darin bestehend, dass er Oxalsäureester mit anderen zweibasischen Estern in Gegenwart von Natriumäthylat zusammenbrachte. Derart gelangte er durch Condensation von Oxalsäureester mit Glutarsäureester zum Ester der Diketopentamethylendicarbonsäure, den er durch Hydrolyse in Diketopentamethylen überführte:

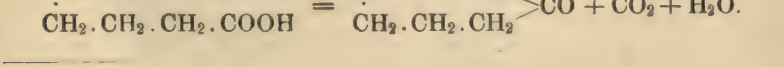


Ferner[2]) condensirte er β,β-Dimethylglutarsäureester mit Oxalsäureester und erhielt Dimethyldiketopentamethylendicarbonsäureester, den Komppa[3]) durch Reduction in Dimethylpentamethylendicarbonsäureester überführte. Dieser Letztere erwies sich als identisch mit Apocamphersäure.

Diese interessante und wichtige Synthese lässt sich folgendermaassen veranschaulichen:



VII. Ringförmige Ketone lassen sich auch durch Destillation der Calciumsalze zweibasischer Säuren gewinnen, wie zuerst durch Boussingault[4]) und nachher von Tilley[5]), sowie Dale und Schorlemmer[6]) an der Korksäure gezeigt wurde. Es ist nunmehr bekannt, dass das Suberon, welches durch Destillation des Calciumsalzes der Korksäure erhalten wird, nichts anderes ist als das Ketoheptamethylen, d. i. das Keton des 7-gliedrigen Kohlenstoffringes:



[1]) Dieckmann, diese Berichte **30**, 1470 [1897].
[2]) Dieckmann, diese Berichte **32**, 1933 [1899].
[3]) Komppa, diese Berichte **34**, 2472 [1902].
[4]) Boussingault, Ann. d. Chem. **19**, 308.
[5]) Tilley, Ann. d. Chem. **39**, 166.
[6]) Dale und Schorlemmer, Ann. d. Chem. **199**, 147.

Diese Reaction wurde nicht weiter untersucht, bis Wislicenus[1]), sowie Baeyer[2]) und seine Schüler mit der Verwerthung dieser Methode nach verschiedenen Richtungen hin sich beschäftigten. Durch Destillation von adipinsaurem Calcium wurde Ketopentamethylen, aus dem Calciumsalz der Pimelinsäure das Ketohexamethylen und aus dem Calciumsalz der Azelaïnsäure das Ketooctomethylen dargestellt:

$$\begin{matrix}CH_2.CH_2.CO_2\\CH_2.CH_2.CO_2\end{matrix}\!\!>\!Ca \text{ liefert } \begin{matrix}CH_2.CH_2\\CH_2.CH_2\end{matrix}\!\!>\!CO.$$

$$CH_2\!<\!\begin{matrix}CH_2.CH_2.CO_2\\CH_2.CH_2.CO_2\end{matrix}\!\!>\!Ca \text{ liefert } CH_2\!<\!\begin{matrix}CH_2.CH_2\\CH_2.CH_2\end{matrix}\!\!>\!CO.$$

$$CH_2\!<\!\begin{matrix}CH_2.CH_2.CH_2.CO_2\\CH_2.CH_2.CH_2.CO_2\end{matrix}\!\!>\!Ca \text{ liefert } CH_2\!<\!\begin{matrix}CH_2.CH_2.CH_2\\CH_2.CH_2.CH_2\end{matrix}\!\!>\!CO.$$

VIII. In einigen besonderen Fällen beobachtete man Reactionen, welche zur Bildung geschlossener Kohlenstoffketten führten, jedoch noch weiterer Untersuchung bedürfen, um allgemeiner anwendbar zu werden. Von diesen sei hier die Synthese von Trimethylendicarbonsäure durch Einwirkung von alkoholischem Kali auf Bromglutarsäureester[3]), oder von Dimethyltrimethylendicarbonsäure (Caronsäure) aus Bromdimethylglutarsäure[4]) erwähnt:

$$CH_2\!<\!\begin{matrix}CH\,Br.CO_2C_2H_5\\CH_2.CO_2C_2H_5\end{matrix} \text{ liefert } CH_2\!<\!\begin{matrix}CH.CO_2H\\CH.CO_2H\end{matrix}$$

$$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C\!<\!\begin{matrix}CH\,Br.CO_2C_2H_5\\CH_2.CO_2C_2H_5\end{matrix} \text{ liefert } \begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C\!<\!\begin{matrix}CH.CO_2H\\CH.CO_2H\end{matrix}.$$

Die Bildung von Caronsäure aus Bromdimethylglutarsäureester ist vielleicht weniger bemerkenswerth, da der Austritt von Bromwasserstoff von vornherein die Schliessung eines Trimethylenringes bedingt; andererseits jedoch muss die Ueberführung von Bromglutarsäureester in Trimethylendicarbonsäureester als unerwartete Ringschliessung bezeichnet werden, da die Reaction eher zur Glutaconsäure, $CO_2H.CH_2.CH{:}CH.CO_2H$, hätte führen sollen, die jedoch nicht einmal spurenweise nachgewiesen wurde.

Eine ähnliche Beobachtung zeigt sich in der quantitativen Bildung von Acetyltrimethylen durch Einwirkung von Kalilauge auf Acetylpropylbromid[5]).

$$CH_3.CO.CH_2\!<\!\begin{matrix}CH_2\\CH_2\,Br\end{matrix} \longrightarrow CH_3.CO.CH\!<\!\begin{matrix}CH_2\\CH_2\end{matrix}.$$

[1]) Wislicenus, Ann. d. Chem. 275, 312 und 364.

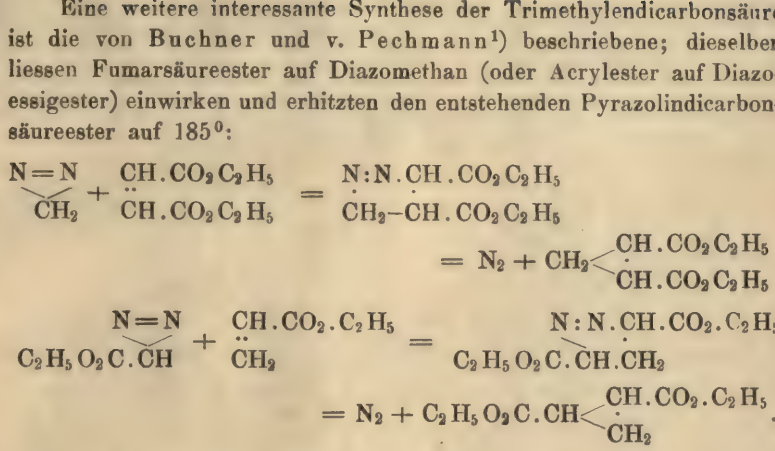
[2]) Baeyer, diese Berichte 26, 229 [1893]; Ann. d. Chem. 178, 112; cf. Mayer, Ann. d. Chem. 275, 362.

[3]) Bowtell und Perkin, Proc. Chem. Soc. 1899, 241.

[4]) Perkin und Thorpe, Soc. 75, 48.

[5]) Idzkowska und Wagner, Centralbl. 1898, II, 474.

Eine weitere interessante Synthese der Trimethylendicarbonsäure ist die von Buchner und v. Pechmann[1]) beschriebene; dieselben liessen Fumarsäureester auf Diazomethan (oder Acrylester auf Diazoessigester) einwirken und erhitzten den entstehenden Pyrazolindicarbonsäureester auf 185°:



Die physikalischen Eigenschaften von Verbindungen gesättigter geschlossener Kohlenstoffketten im Vergleich mit denen von Verbindungen gesättigter und ungesättigter offener Kohlenstoffketten.

Eines der augenfälligsten Momente bei Betrachtung der physikalischen Eigenschaften von Verbindungen mit gesättigten geschlossenen Kohlenstoffketten ist, dass dieselben bei höherer Temperatur sieden und höheres specifisches Gewicht haben, als einerseits die ungesättigten Verbindungen, mit denen sie isomer sind, und andererseits die gesättigten Verbindungen, welche zwei Atome Wasserstoff mehr enthalten. Dies ist aus den beiden Tabellen A und B (auf S. 2102) ersichtlich, welche diese Eigenschaften für Kohlenwasserstoffe und Carbonsäuren angeben, soweit sie ermittelt worden sind.

Noch grössere Unterschiede zeigt eine Gegenüberstellung des magnetischen Drehungsvermögens von gesättigten Ringverbindungen und dem der entsprechenden ungesättigten Verbindungen mit offenen Kohlenstoffketten. Einige wenige Beispiele mögen dies veranschaulichen[2]):

	Magnet. Dreh.	
Hexamethylen, C_6H_{12}	5.664	1.809.
Hexylen, C_6H_{12} (Methylpropyläthylen) . .	7.473	

Bei diesen Kohlenwasserstoffen differirt also der Werth der magnetischen Drehung für die Ringverbindungen um 1.809 von dem der isomeren, ungesättigten, offenen Kette.

[1]) Buchner, diese Berichte 23, 703; Buchner und Papendieck, Ann. d. Chem. 284, 212; v. Pechmann, diese Berichte 27, 1891.

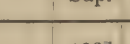
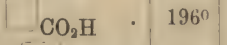
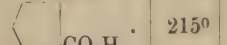
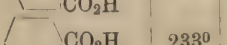
[2]) Perkin sen., Soc. 81, 292.

Tabelle A. Kohlenwasserstoffe.

	Sdp.	Sp. Gw.		Sdp.	Sp. Gw.		Sdp.	Sp. Gw.
Trimethylen, $CH_2<\begin{matrix}CH_2\\CH_2\end{matrix}$	−35°		Propan, $CH_3.CH_2.CH_3$	−39°		Propylen, $CH_3.CH:CH_2$	−50°	
Tetramethylen (unbekannt)								
Methyltrimethylen, $CH_3.CH<\begin{matrix}CH_2\\CH_2\end{matrix}$ . . .	+ 5°		Butan, $CH_3.CH_2.CH_2.CH_3$	+ 1°	0.600[3]	Butylen, $CH_3.CH_2.CH:CH_2$	− 5°	
Pentamethylen, $CH_2<\begin{matrix}CH_2.CH_2\\CH_2.CH_2\end{matrix}$	50.8°	0.7506[1]	Pentan, $CH_3.CH_2.CH_2.CH_2.CH_3$	36.3°	0.627[4]	Amylen, $CH_3.CH_2.CH_2.CH:CH_2$	40°	
Hexamethylen, $CH_2<\begin{matrix}CH_2.CH_2\\CH_2.CH_2\end{matrix}>CH_2$ . .	80.8°	0.7823[2]	Hexan, $CH_3.CH_2.CH_2.CH_2.CH_2.CH_3$	68.9°	0.658[5]	Methyl-propyläthylen	68°	0.6997[3]

[1]) bei $\frac{20.5°}{4}$ [2]) bei $\frac{15°}{4}$ [3]) bei 0° [4]) bei 14° [5]) bei 0°

Tabelle B. Carbonsäuren.

	Sdp.	Sp. Gw.		Sdp.	Sp. Gw.		Sdp.	Sp. Gw.
Trimethylencarbonsäure,  . .	182°	1.092[1]	Buttersäure . .	162°	0.978[3]	Vinylessigsäure	168°	
Tetramethylencarbonsäure, .	196°	1.055	Valeriansäure .	185°	0.956[3]	Allylessigsäure	189°	0.984[1]
Pentamethylencarbonsäure,  .	215°	1.054[2]	Capronsäure .	205°	0.945[3]	Hydrosorbinsäure	208°	0.964[5]
Hexamethylencarbonsäure,  .	233°		Oenanthylsäure	223°	0.931[3]	Heptylensäure	228°	
Heptamethylencarbonsäure, 	248°		Caprylsäure .	236°	0.911[4]			

[1]) bei 15° [2]) bei 4° [3]) bei 0° [4]) bei 20° [5]) bei $\frac{23°}{4}$

Eine ganz ähnliche, wenngleich etwas geringere Differenz ist bei den Carbonsäuren zu verzeichnen:

	Magnet. Dreh.	
Trimethylencarbonsäure	4.141	1.262
Vinylessigsäure (berechnet durch Subtraction des Werthes für CH_2 vom Werthe der Allylessigsäure)	5.403	

ferner:

	Magnet. Dreh.	
Tetramethylencarbonsäure	5.048	1.378.
Allylessigsäure	6.426	

Der Unterschied bei den Säuren ist also zwischen Ringverbindungen und isomeren Säuren mit ungesättigten, offenen Ketten etwa 1.3.

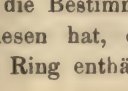
Wie werthvoll sich die Bestimmung der magnetischen Drehung für die Beurtheilung erwiesen hat, ob eine vorliegende Verbindung ungesättigt ist oder einen Ring enthält, wird noch später beleuchtet werden.

Die relative Leichtigkeit der Ringbildung und relative Beständigkeit der Ringe.

(Baeyer's »Spannungs-Theorie«.)

Einer der interessantesten und werthvollsten Gesichtspunkte in Bezug auf die Bildung und Beständigkeit der Ringe ist in der Baeyerschen Spannungs-Theorie niedergelegt, welche im Jahre 1885 [1]) veröffentlicht wurde. Dieselbe ist kurzgefasst die Folgende:

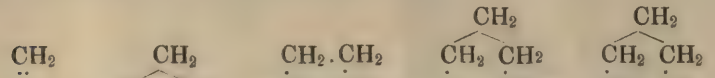
Angenommen, dass die vier Affinitäten des Kohlenstoffes in den Richtungen der Achsen wirken, welche man sich vom Mittelpunkt eines Tetraëders zu den Ecken desselben geführt denkt, so schliessen dieselben unter einander einen Winkel von 109° 28' ein. Verbinden sich nun Kohlenstoffatome zu einer geschlossenen Kette, so ändern sich damit die Richtungen dieser Affinitäten, und es entsteht eine »Spannung«, welche sich messen lässt durch den Winkel der Affinitäts-Ablenkung. Für den Trimethylenring, $\overset{CH_2}{\diagup\diagdown}$ $CH_2.CH_2$ z. B., dessen Kohlenstoffatome als die Ecken eines gleichseitigen Dreieckes gedacht werden können, beträgt der Winkel, den die Affinitätsrichtungen der Kohlenstoffatome einschliessen, 60°, die Ablenkung eines jeden daher $\frac{1}{2}$ (109° 28' — 60°) = 24° 44', beim Tetramethylenring,



hingegen ist sie nur $\frac{1}{2}$ (109° 28' — 90°) = 9° 44'. Die folgende Tabelle, welche der Baeyer'schen Abhandlung entnommen ist, giebt

[1]) Baeyer, diese Berichte 18, 2277 [1885]

die Ablenkung der Affinitäten der Kohlenstoffatome bei der Bildung der verschiedenen Kohlenstoffringe:



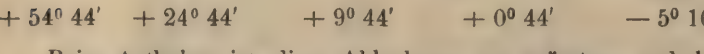
+ 54° 44′	+ 24° 44′	+ 9° 44′	+ 0° 44′	— 5° 16′.

Beim Aethylen ist diese Ablenkung am grössten, und das Bestreben des Ringes, sich unter Bildung von Additionsverbindungen zu öffnen, sollte deshalb ein sehr ausgeprägtes sein; in der That zeigte sich dies experimentell bestätigt, indem sich Aethylen leicht mit Bromwasserstoff, Brom, Chlor und selbst mit Jod combinirt.

Beim Trimethylen ist die Ablenkung weit geringer, und wenn auch dieses Gas noch mit Bromwasserstoff und mit Brom unter Aufbrechung des Ringes sich verbindet, so geschieht dies ungemein schwerer als beim Aethylen.

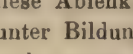
In Uebereinstimmung mit Baeyer's Theorie sollte der Tetramethylenring viel beständiger sein als der Trimethylenring, was klar bewiesen ist durch die relativen Eigenschaften einiger Verbindungen dieser Kohlenwasserstoffe.

Trimethylencarbonsäure z. B. reagirt leicht mit Bromwasserstoffsäure unter Bildung von γ-Brombuttersäure:



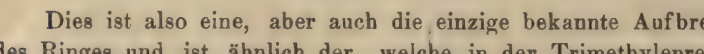
$$CH_2.CH.CO_2H + HBr = CH_2Br.CH_2.CH_2.CO_2H,$$

während andererseits die Tetramethylencarbonsäure,



von Bromwasserstoffsäure unter ähnlichen Bedingungen kaum angegriffen wird.

Doch ist diese Beständigkeit des Tetramethylenringes nur eine verhältnissmässige, da gefunden wurde, dass Hydroxytetramethylen unter der Einwirkung von Bromwasserstoffsäure, neben Bromtetramethylen, zugleich 1.3-Dibrombutan[1]) ergiebt.



$$CH_2.CH(OH) \longrightarrow CH_2.CHBr \text{ und } CH_3.CHBr.CH_2.CH_2Br.$$

Dies ist also eine, aber auch die einzige bekannte Aufbrechung des Ringes und ist ähnlich der, welche in der Trimethylenreihe so häufig beobachtet wurde.

[1]) Perkin, Soc. 65, 951.

Pentamethylencarbonsäure, sowie Hexamethylencarbonsäure,

$$CH_2\begin{<}{l}CH_2.CH_2\\CH_2.CH.CO_2H\end{>} \quad \text{und} \quad CH_2\begin{<}{l}CH_2.CH_2\\CH_2.CH_2\end{>}CH.CO_2H,$$

werden anscheinend selbst bei langem Kochen mit Bromwasserstoffsäure nicht angegriffen. Bezüglich der Beständigkeit des 7- und 8-Kohlenstoffringes ist nahezu nichts bekannt.

Wenn wir uns nunmehr der anderen Seite der Frage zuwenden und die Leichtigkeit, mit welcher die Ringe geformt werden, vom Gesichtspunkt der Baeyer'schen Theorie in's Auge fassen, so begegnen wir der Schwierigkeit, dass das bis jetzt vorhandene Beweismaterial nicht genügend ist, um definitive Schlüsse daraus zu ziehen.

Bei der Einwirkung von Natrium-Malonester auf Aethylen-, Methyltetramethylen-, Pentamethylen- und Hexamethylen-Dibromid, welche zu Verbindungen des 3-, 4-, 5-, 6- und 7-Kohlenstoff-Ringes führt, wurde beobachtet, dass der 5-Kohlenstoffring sich fast quantitativ bildet, während der 4-Kohlenstoffring in geringerer und der 3-Kohlenstoffring in noch schlechterer Ausbeute entsteht. Der 6-Kohlenstoffring wieder ging in schlechterer Ausbeute als der 5 Kohlenstoffring hervor, bedeutend schlechter, als die geringe Spannungs-Differenz erwarten liess. Der 7-Kohlenstoffring entstand unter ausserordentlicher Schwierigkeit. Die Ausbeute der Heptamethylenverbindung, welche durch Einwirkung von Hexamethylendibromid auf Natriummalonester dargestellt wurde, war äusserst gering; was endlich den 8-Kohlenstoffring anbelangt, so liessen sich durch Destillation des Calciumsalzes der Azelaïnsäure nur Spuren von Ketooctomethylen erhalten. Aehnliche Beobachtungen sind auch bei anderen Ringsynthesen gemacht worden.

Sofern sich auf diese Versuche ein Urtheil basiren lässt, lautet dasselbe dahin, dass die »Spannungs-Theorie« genauer ist und der Wahrheit näher kommt in Bezug auf die positiven Spannungswinkel, z. B. beim Aethylen, Trimethylen, Tetramethylen und Pentamethylen, als in Bezug auf die Beständigkeit von Kohlenstoffringen, für welche ein negativer Spannungswinkel in Frage kommt, wie dies beim Hexamethylen, Heptamethylen, Octomethylen u. s. w. der Fall ist.

Weiteres werthvolles Beweismaterial für die Giltigkeit der Spannungstheorie ergiebt sich aus den Verbrennungswärmen von Verbindungen der gesättigten 3-, 4-, 5- und 6-Kohlenstoffringe [1]).

Vergleicht man die so erhaltenen Werthe mit denen der entsprechenden aliphatischen Verbindungen, welche zwei Wasserstoffatome mehr enthalten, so lässt sich der Energieverlust infolge der Ring-

[1]) Stohmann, Journ. für prakt. Chem. [2] 45, 489 [1892]; vergl. Meyer und Jacobson, Lehrbuch der organischen Chemie, Band II, 7.

spaltung und der Wasserstoffaufnahme leicht berechnen. Er beträgt z. B. für den

Trimethylenring	37.1 Cal.
Tetramethylenring	39.9 »
Pentamethylenring	16.1 »
Hexamethylenring	14.3 »

Dies stimmt allgemein mit der Spannungstheorie überein.

Ich will nun die Charakteristik der einzelnen Ringe zum Gegenstand der weiteren Besprechung machen.

Der Trimethylenring.

Unter allen bisher näher untersuchten Ringen ist der Trimethylenring in vielfacher Hinsicht der interessanteste, hauptsächlich wegen seiner merkwürdigen Beständigkeits-Verhältnisse und wegen der Aehnlichkeit seiner Verbindungen mit den Verbindungen der ungesättigten offenen Kohlenstoffketten.

Um dies zu erläutern, seien im Folgenden nur die Beständigkeitsbedingungen für

Trimethylen, $CH_2\langle\begin{matrix}CH_2\\CH_2\end{matrix}$,

Trimethylendicarbonsäure, $\begin{matrix}CH_2\\CH_2\end{matrix}\rangle C(CO_2H)_2$,

Trimethylenmonocarbonsäure, $\begin{matrix}CH_2\\CH_2\end{matrix}\rangle CH(COOH)$

und

Acetyltrimethylen, $\begin{matrix}CH_2\\CH_2\end{matrix}\rangle CH.CO.CH_3$

in Betracht gezogen.

Trimethylen, $\begin{matrix}CH_2\\CH_2\end{matrix}\rangle CH_2$.

Freund[1]), der diesen interessanten Kohlenwasserstoff entdeckte, zeigte, dass er sich leicht mit Jodwasserstoff verbindet unter Bildung von Propyljodid,

$$\begin{matrix}CH_2\\CH_2.CH_2\end{matrix}\rangle + HJ = CH_3.CH_2.CH_2J,$$

und dass er von Schwefelsäure leicht aufgenommen wird unter Aufbrechung des 3-Kohlenstoffringes und Bildung von normalem Propylsulfat,

$$(CH_3.CH_2.CH_2)_2SO_4;$$

[1]) Freund, Monatsh. für Chem. 3, 626.

dass er andererseits von Brom nur langsam angegriffen wird, wobei Trimethylendibromid entsteht,

$$BrCH_2.CH_2.CH_2Br.$$

Diese Zersetzungen unterscheiden das Trimethylen sehr scharf vom Propylen, $CH_3.CH{:}CH_2$, da dieses unter gleicher Behandlung Isopropyljodid, $CH_3.CHJ.CH_3$, Isopropylsulfat, $[(CH_3)_2.CH]_2SO_4$ und Propylendibromid, $CH_3.CHBr.CH_2Br$, liefert.

Trimethylen ist also ein Kohlenwasserstoff, der wohl viele Eigenschaften mit den ungesättigten Substanzen gemein hat, aber dennoch vom Propylen sehr verschieden ist. In allen Umsetzungen, in denen es Additionsproducte giebt, zeigt Trimethylen (auch in seinen Verbindungen) die Eigenschaften eines α-γ-ungesättigten Kohlenwasserstoffes, so z. B. in seinem Verhalten gegen Brom- und Jod-Wasserstoffsäure:

$$\begin{array}{ccccccc} CH_2 & & CH_2. & & CH_2Br & & CH_2H \\ \diagup\!\diagdown & \longrightarrow & \diagup\!\diagdown & \longrightarrow & \diagup\!\diagdown & \longrightarrow & \diagup\!\diagdown \\ CH_2.CH_2 & & CH_2.CH_2. & & CH_2.CH_2Br & & CH_2.CH_2J \end{array}.$$

Mit Brom verbinden sich Trimethylen und seine Derivate nur äusserst langsam und unterscheiden sich daher in dieser Beziehung besonders scharf von den gewöhnlichen ungesättigten Substanzen. Man nimmt daher an, dass das Trimethylen gesättigt ist, und dies wird auch durch die Beobachtung Wagner's[1]) unterstützt, welcher zeigte, dass das Trimethylen in der Kälte Permanganat nicht reducirt.

Ziehen wir nun die Trimethylendicarbonsäure in Betracht,

$$\begin{matrix} CH_2 \\ CH_2 \end{matrix}\!\!>\!C(CO_2H)_2,$$

so finden wir, dass auch diese Säure, wiewohl sie in ihren meisten Umsetzungen den Charakter einer ungesättigten Substanz zeigt, nichtsdestoweniger als eine gesättigte Verbindung bezeichnet werden muss.

Der Ester dieser Säure wird durch Einwirkung von Aethylendibromid auf Natriummalonester dargestellt, wobei sich muthmaasslich eine Reaction in zwei Stadien abspielt — entweder unter Bildung eines Ringes:

$$(CO_2C_2H_5)_2CHNa + BrCH_2.CH_2Br = (CO_2C_2H_5)CH.CH_2.CH_2Br + NaBr,$$

$$(CO_2C_2H_5)_2CNa.CH_2.CH_2Br = (CO_2C_2H_5)_2C\!\!<\!\!\begin{matrix} CH_2 \\ CH_2 \end{matrix} + NaBr,$$

oder aber (infolge Austritts von Bromwasserstoff aus dem zuerst gebildeten Brompropylmalonester) unter Bildung des ungesättigten Vinylmalonesters,

$$(CO_2C_2H_5)_2CH.CH{:}CH_2.$$

[1]) Wagner, diese Berichte 21, 1236 [1888].

Durch Hydrolyse des Reactionsproductes lässt sich eine schön krystallisirende zweibasische Säure $C_3H_4(CO_2H)_2$ erhalten, welche sich demnach entweder als

Trimethylendicarbonsäure, $\begin{matrix}CH_2\\ \dot{}\\ CH_2\end{matrix}\!\!>\!C(CO_2H)_2$,

oder als

Vinylmalonsäure, $(CO_2H)_2CH.CH:CH_2$,

ansprechen lässt.

Lange Zeit herrschten betreffs der Constitution dieser Säure verschiedene Ansichten.

Fittig[1]) vertrat die Anschauung, dass es sich um eine ungesättigte Säure der zweiten Constitution handle, während der Vortragende auf Grund der Bestimmung der magnetischen Drehung den Standpunkt einnahm, dass die Trimethylendicarbonsäure[2]) vorliege.

Die Säure zeigt allerdings im höchsten Grade die Eigenschaften einer ungesättigten Substanz. In der Kälte mit rauchender Bromwasserstoffsäure behandelt, geht sie sofort in die γ-Bromäthylmalonsäure[3]) über, in welcher das Bromatom in der γ-Stellung steht, da die Säure durch Kochen mit Wasser unter Kohlensäureentwickelung in Butyrolacton übergeht:

$$\begin{matrix}CO_2H.\dot{C}H.CH_2.\dot{C}H_2\\ \dot{}\quad\quad\dot{}\\ CO_2H\quad Br\end{matrix} = CO_2 + \begin{matrix}CH_2.CH_2.\dot{C}H_2\\ \dot{}\quad\quad\quad\dot{}\\ CO\text{———}O\end{matrix} + HBr.$$

Ferner nimmt die Säure $C_3H_4(CO_2H)_2$ langsam Brom auf und bildet dabei Dibromäthylmalonsäure, $C_3H_4Br_2(CO_2H)_2$[4]), während sie weiterhin durch einfache Destillation unter Kohlensäureabspaltung theils in Butyrolacton, theils in die einbasische Säure $C_3H_5.CO_2H$ zerlegt wird; beim Kochen mit verdünnter Schwefelsäure hingegen wird sie zum grössten Theile unter Bildung von Butyrolacton zersetzt.

Alle diese Reactionen sind höchst charakteristisch für ungesättigte Säuren mit der Doppelbindung in der β-γ- (oder γ-δ-) Stellung, und deshalb ist es gar nicht überraschend, dass die Säure $C_3H_4(CO_2H)_2$ und die monobasische Säure $C_3H_5(CO_2H)$, welche sich aus ihr durch Destillation erhalten lässt, als ungesättigte Säuren angesehen wurden.

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[1]) Fittig, Ann. d. Chem. **227**, 25.

[2]) Perkin, diese Berichte **17**, 54 und 323 [1884].

[3]) Eine solche Umsetzung wäre aber ungewöhnlich, wenn die Säure Vinylmalonsäure, $(CO_2H)_2CH.CH:CH_2$, wäre, da in diesem Falle die Anlagerung der Bromwasserstoffsäure eher unter Bildung von β-Bromäthylmalonsäure, $(CO_2H)_2CH.CHBr.CH_3$, vor sich gehen würde; giebt doch die Allylmalonsäure, $(CO_2H)_2CH.CH_2.CH:CH_2$, mit Bromwasserstoffsäure γ-Brompropylmalonsäure, $(CO_2H)_2CH.CH_2.CHBr.CH_3$.

[4]) Marburg, Ann. d. Chem. **294**, 125.

Anderseits lässt sich die Säure $C_3H_4(CO_2H)_2$ durch Natriumamalgam nicht reduciren und reducirt auch Permanganat in sodaalkalischer Lösung nicht[1]). Sie unterscheidet sich von ungesättigten Säuren weiterhin dadurch, dass sie selbst von der stärksten Salpetersäure in der Kälte nicht verändert wird[2]).

Es war aber die Bestimmung der magnetischen Drehung des Esters der Säure $C_3H_4(CO_2H)_2$, welche den ersten Beweis lieferte, dass diese Säure unmöglich Vinylmalonsäure sein konnte, sondern dass sie als Trimethylendicarbonsäure aufgefasst werden musste. Das magnetische Drehungsvermögen wurde gleich 9.166 gefunden. Wäre der Ester Vinylmalonester,

$$(CO_2C_2H_5)_2CH.CH{:}CH_2,$$

so liesse sich sein magnetisches Drehungsvermögen leicht aus dem des Allylmalonesters,

$$(CO_2C_2H_5)_2CH.CH_2.CH{:}CH_2 \quad (11.281),$$

durch Subtraction des Werthes für CH_2 (1.023) berechnen und würde sich auf 10.258 beziffern. Diese Zahl ist um 1.092 höher als die experimentell für den Ester der Säure $C_3H_4(CO_2H)_2$ gefundene; die Säure kann also unmöglich Vinylmalonsäure sein und muss daher als Trimethylendicarbonsäure,

$$\begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix}\!\!>\!C(CO_2H)_2,$$

aufgefasst werden.

Aehnlich ergiebt sich die Constitution der Säure $C_3H_5.CO_2H$, welche aus der oben genannten Dicarbonsäure durch Destillation erhältlich ist.

Die gefundene magnetische Drehung derselben beträgt 4.141; nach Abzug des CH_2-Werthes (1.023) vom magnetischen Drehungsvermögen der Allylessigsäure, $CO_2H.CH_2.CH_2.CH{:}CH_2$ (6.426), erhält man 5.403 für Vinylessigsäure, $CO_2H.CH_2.CH{:}CH_2$, welche Zahl um 1.262 höher ist als die für die Säure $C_3H_5.CO_2H$ wirklich gefundene. Die Säure ist deshalb keinesfalls Vinylessigsäure, sondern Trimethylencarbonsäure,

$$\begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix}\!\!>\!CH.CO_2H.$$

Späterhin[3]) wurde eine bemerkenswerthe Eigenschaft der Trimethylendicarbonsäure aufgefunden, welche ihre Constitution thatsäch-

[1]) Buchner, diese Berichte **23**, 704 [1890].
[2]) Franchimont, diese Berichte **19**, 1051 [1886].
[3]) Bone und Perkin, Soc. **67**, 108.

lich klarlegte, die bis dahin hauptsächlich durch physikalische Betrachtungen gestützt war. Wird nämlich Trimethylendicarbonsäureester in alkoholischer Lösung mit Natriummalonester behandelt, so bildet sich durch einfache Addition Butantetracarbonsäureester:

$$(CO_2C_2H_5)_2CH_2 + \begin{matrix}CH_2\\ \dot{}\\ CH_2\end{matrix}\!\!>\!C(CO_2C_2H_5)_2 = \begin{matrix}CH_2.CH(CO_2C_2H_5)_2\\ \dot{}\\ CH_2.CH(CO_2C_2H_5)_2\end{matrix}.$$

Dass demselben wirklich diese Constitution zukommt, war dadurch bewiesen, dass er bei Behandlung mit concentrirter Salzsäure leicht und nahezu quantitativ in Adipinsäure übergeht. Abgesehen von der Unwahrscheinlichkeit, dass ein ungesättigter Ester von der Formel: $CH_2:CH.CH(CO_2C_2H_5)_2$ mit Natriummalonester ein Additionsproduct ergeben würde, lässt sich die Bildung von Butantetracarbonsäureester in erwähnter Weise kaum anders als durch die Annahme erklären, dass der Ausgangsester einen Trimethylenring enthält. Der Trimethylendicarbonsäureester verhält sich bei dieser Reaction als ein α,γ-ungesättigter Ester:

$$\begin{matrix}\overset{\beta}{CH_2}\\ \dot{}\\ \underset{\gamma}{CH_2}\end{matrix}\!\!>\!\underset{\alpha}{C}(CO_2C_2H_5)_2 = \underset{\gamma}{\dot{C}H_2}.CH_2.\underset{\alpha}{\dot{C}}(CO_2C_2H_5)_2.$$

Von diesem Gesichtspunkte aus betrachtet, zeigt sich die Addition von Malonsäureester bei der Bildung von Butantetracarbonsäureester vollkommen klar und durch folgende Gleichung darstellbar:

$$(CO_2C_2H_5)_2CHH + \dot{C}H_2.CH_2.\dot{C}(CO_2C_2H_5)_2 = (CO_2C_2H_5)_2CH.CH_2.CH_2.CH(CO_2C_2H_5)_2.$$

Es liesse sich schwerlich eine andere Auffassung dieser interessanten Reaction finden, und diese Synthese des Butantetracarbonsäureesters erscheint daher als weiterer Beweis dafür, dass der verwendete Ester ein Trimethylendicarbonsäureester ist.

Wenden wir uns nunmehr dem Acetyltrimethylen,

$$\begin{matrix}CH_2\\ \dot{}\\ CH_2\end{matrix}\!\!>\!CH.CO.CH_3,$$

zu, so finden wir, dass diese Substanz in noch ausgeprägterem Maasse als das Trimethylen und die Trimethylen-1.1-dicarbonsäure oder Trimethylenmonocarbonsäure die Eigenschaften einer ungesättigten Verbindung besitzt.

Zur Darstellung dieses Ketons lässt man Acetessigester auf Aethylenbromid[1]) einwirken, wobei die Reaction vermuthlich wiederum in zwei Stadien verläuft:

$$\begin{aligned} &CH_3.CO \\ &CO_2C_2H_5.CHNa + BrCH_2.CH_2Br \\ &\qquad\qquad\qquad CH_3.CO \\ &\quad = CO_2C_2H_5.CH.CH_2.CH_2Br + NaBr, \end{aligned}$$

Bromäthylacetessigester

$$\begin{aligned} CH_3.CO \quad CH_2 \qquad\qquad CH_3.CO \quad CH_2 \\ CO_2C_2H_5.C\,Na \quad CH_2Br = CO_2C_2H_5.C\!-\!CH_2 + NaBr. \end{aligned}$$

Der so erhaltene Acetyltrimethylencarbonsäureester geht durch Hydrolyse in Acetyltrimethylencarbonsäure,

$$CH_3.CO.C.COOH$$
$$CH_2\!-\!CH_2,$$

und diese durch Destillation unter Kohlensäureabspaltung in Acetyltrimethylen über:

$$CH_3.CO.CH<\begin{matrix}CH_2\\CH_2\end{matrix},$$

ein farbloses Oel, welches bei 112—113° siedet und das Verhalten eines Ketons zeigt, da es bei Behandlung mit Hydroxylamin ein Oxim

$$CH_3.C(:N.OH)CH<\begin{matrix}CH_2\\CH_2\end{matrix}$$

liefert.

Acetyltrimethylen lässt sich auch nahezu quantitativ aus Acetylpropylbromid, $CH_3.CO.CH_2.CH_2.CH_2Br$, mittels festem Kali erhalten[2]). Aus diesem Umstande und in Folge der Darstellung aus Acetessigester konnte der Schluss gezogen werden, dass ein ungesättigtes Keton von der Formel $CH_3.CO.CH_2.CH:CH_2$ vorliegt, also Vinylaceton.

Thatsächlich zeigt das Acetyltrimethylen in seinem Verhalten gegenüber verschiedenen Reagentien alle Eigenthümlichkeiten einer ungesättigten Substanz, so z. B. wird es durch rauchende Bromwasserstoffsäure in Acetylpropylbromid,

$$CH_3.CO.CH_2.CH_2.CH_2Br,$$

durch Kochen mit verdünnter Salzsäure in Acetopropylalkohol,

$$CH_3.CO.CH_2.CH_2.CH_2.OH,$$

---

[1]) Perkin, diese Berichte 17, 1441 [1884].

[2]) Idzkowska und Wagner, Centralblatt 1898, II, 474. — Lipp, diese Berichte 22, 1207 [1889].

und, was am beachtenswerthesten ist, durch Reduction mit Natriumamalgam in Methylpropylcarbinol,

$$CH_3.CH(OH).CH_2.CH_2.CH_3,$$

übergeführt.

Doch, entgegen diesen Beobachtungen, beweisen die bei der Bestimmung des magnetischen Drehungsvermögens von Acetyltrimethylen erhaltenen Resultate, dass unmöglich das Vinylaceton,

$$CH_3.CO.CH_2.CH:CH_2,$$

vorliegen kann.

Dasselbe wurde zu 5.245 festgestellt, während man das Drehungsvermögen von Vinylaceton — vom Allylaceton ausgehend — rechnerisch zu 6.372 findet, was also eine Differenz von 1.127 ergiebt.

Dieser auf physikalische Messungen gestützte Constitutionsbeweis des Acetyltrimethylens wurde nachher von Idzkowska und Wagner[1]) bestätigt, welche zeigten, dass Acetyltrimethylen durch Behandlung mit Permanganat vorerst zu Trimethylenglyoxylsäure und darauf zu Trimethylencarbonsäure oxydirt wird:

$$\begin{matrix}CH_2\\CH_2\end{matrix}\!\!>\!CH.CO.CH_3 \longrightarrow \begin{matrix}CH_2\\CH_2\end{matrix}\!\!>\!CH.CO.CO_2H$$

$$\longrightarrow \begin{matrix}CH_2\\CH_2\end{matrix}\!\!>\!CH.CO_2H.$$

Beim Vergleich der Trimethylen-1.2-dicarbonsäure,

$$CH_2\!<\!\begin{matrix}CH.CO_2H\\CH.CO_2H\end{matrix},$$

mit der 1.1-Dicarbonsäure,

$$CH_2\!<\!\begin{matrix}CH_2\\C(CO_2H)_2\end{matrix},$$

ist ein enormer Unterschied der Stabilitäts-Eigenschaften erkennbar. Die 1.2-Säure wurde zuerst von Conrad und Guthzeit[2]) erhalten. Dieselben liessen Natriummalonester auf α,β-Dibrompropionsäureester einwirken:

$$(CO_2C_2H_5)_2CNa_2 + \begin{matrix}Br.CH_2\\Br.CH.CO_2C_2H_5\end{matrix}$$

$$= (CO_2C_2H_5)_2C\!<\!\begin{matrix}CH_2\\CH.CO_2C_2H_5\end{matrix} + 2\,NaBr,$$

und gelangten von diesem durch Hydrolyse und Kohlensäureeliminirung zur Trimethylen-1.2-dicarbonsäure, welche in der *cis*- und *trans*-

[1]) loc. cit.

[2]) Conrad Guthzeit, diese Berichte **17**, 1187 [1884]; vergl. Buchner, diese Berichte **23**, 703 [1890].

Form existirt. Erstere schmilzt bei 139° und liefert ein Anhydrid vom Schmp. 59°, während die *trans*-Säure vom Schmp. 175° kein Anhydrid besitzt. Beide Modificationen sind ungemein beständig und werden weder von Bromwasserstoffsäure, Brom, Natriumamalgam oder Permanganat angegriffen. Die *trans*-Säure siedet bei sehr hoher Temperatur ohne Zersetzung, während die *cis*-Säure bei der Destillation glatt in ihr Anhydrid übergeht.

Eine ähnliche Stabilität wurde auch bei den Caronsäuren oder Dimethyltrimethylendicarbonsäuren[1]),

$$(CH_3)_2C<\begin{matrix}CH.CH_2H\\ \vdots\\ CH.CO_2H\end{matrix},$$

sowie bei der Trimethylentricarbonsäure,

$$CO_2H.CH<\begin{matrix}CH.CO_2H\\ \vdots\\ CH.CO_2H\end{matrix},$$

beobachtet.

Es ist nach diesen und anderen Betrachtungen offenbar, dass die Beständigkeit des Trimethylenringes sehr beeinflusst ist durch die Gruppen, mit denen er verbunden ist, doch fehlen noch Untersuchungen über genügend zahlreiche Verbindungen desselben, bevor weitere Schlüsse gezogen werden dürfen.

Erwähnenswerth ist noch die grosses Interesse beanspruchende Methylcyclopropendicarbonsäure, $CH_3.CH<\begin{matrix}C.CO_2H\\ \vdots\\ C.CO_2H\end{matrix}$, welche zuerst von Feist[2]) beschrieben wurde und sich vom ungesättigten Cyclopropen, $CH_2<\begin{matrix}CH\\ \vdots\\ CH\end{matrix}$, ableitet.

Diese Säure wird dargestellt durch Behandeln von Bromisodehydroacetessigester mit Kali, welche Reaction sich folgendermaassen veranschaulichen lässt:

$$\begin{matrix}CH_3.C.O.CO\\ \|\quad\diagdown\\ C_2H_5CO_2.C.C(CH_3):CBr\end{matrix} + 2KOH = \begin{matrix}CH_3.CO\\ |\\ C_2H_5CO_2.CK.C(CH_3):CBr\end{matrix}\quad\begin{matrix}CO_2K\\ |\end{matrix}$$

$$+ H_2O = CH_3.CO_2H + C_2H_5CO_2.\underset{\diagdown\!\!\diagup\ C(CH_3)}{CHK\,CBr}.CO_2K = KBr$$

$$+ C_2H_5CO_2.\underset{\diagdown\!\!\diagup\ C.CH_3.}{CH.C}.CO_2K$$

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[1]) Baeyer und Ipatieff, diese Berichte **29**, 2796 [1896]; Perkin und Thorpe, Soc. **75**, 48.

[2]) Feist, diese Berichte **26**, 750, 759 [1896].

Die freie Säure schmilzt bei 200° und vereinigt sich mit Brom zu einem Dibromid; beim Erwärmen mit Bromwasser jedoch spaltet sich der Ring unter Bildung von Oxalbrombuttersäure auf:

$$CH_3.CH\begin{matrix}\diagup C.CO_2H\\ \diagdown C.CO_2H\end{matrix} + BrOH = CH_3.CH\begin{matrix}\diagup CHBr.CO_2H\\ \diagdown CO.CO_2H.\end{matrix}$$

Sollten weitere Untersuchungen die der Säure von Feist zugeschriebene Constitution ergeben, so wäre der Beweis erbracht, dass der Cyclopropen Ring beständig ist, und damit ein weiterer Beweis für die Beständigkeit des dreigliedrigen Kohlenstoffringes im Allgemeinen.

Der Tetramethylenring.

Der Kohlenwasserstoff Tetramethylen

$$\begin{matrix}CH_2.CH_2\\ CH_2.CH_2\end{matrix}$$

ist noch nicht isolirt worden, obwohl angenommen werden darf, dass er sich durch Reduction von Bromtetramethylen

$$\begin{matrix}CH_2.CH_2\\ CH_2.CHBr,\end{matrix}$$

oder durch Einwirkung von Natrium oder Zink auf Tetramethylendibromid, $BrCH_2.CH_2.CH_2.CH_2Br$, darstellen lassen wird, sobald diese schon bekannten Substanzen in genügender Quantität zugänglich sein werden.

Analogie-Schlüsse lassen voraussetzen, dass er sehr leicht flüchtig sein und bei etwa 20° sieden werde. Es wurden Versuche angestellt, denselben aus Tetramethylencarbonsäure zu erhalten durch Destillation ihres Calciumsalzes mit Kalk[1]); doch hatten diese bisher keinen Erfolg. Eine beträchtliche Quantität eines Gases wurde zwar abgeschieden, doch erwies sich dasselbe fast gänzlich als Aethylen, welches durch Zerfall von Tetramethylen entstanden sein dürfte:

$$\begin{matrix}CH_2.CH_2\\ CH_2.CH_2\end{matrix} = \begin{matrix}CH_2\\ CH_2\end{matrix} + \begin{matrix}CH_2\\ CH_2\end{matrix}$$

Hingegen ist das nächste Homologe des Tetramethylens, das Methyltetramethylen,

$$\begin{matrix}CH_2.CH.CH_3\\ CH_2.CH_2\end{matrix},$$

bekannt. Dasselbe wurde erhalten durch Behandlung von 1.4-Dibrompentan, $CH_3.CHBr.CH_2.CH_2.CH_2Br$, mit Natrium[2]). Es bildet eine

[1]) Colman, Perkin, Soc. 51, 228.
[2]) Colman, Perkin, Soc. 53, 201.

sehr leicht flüchtige Flüssigkeit vom Sdp. 39—42° und wird von Jodwasserstoffsäure bei gewöhnlicher Temperatur nicht angegriffen.

Tetramethylenderivate sind allgemein viel beständiger als Trimethylenverbindungen, und es gelang daher aus der Tetramethylencarbonsäure,

$$\begin{matrix} CH_2.CH_2 \\ CH_2.CH.CO_2H, \end{matrix}$$

unter Heranziehung der für aliphatische Verbindungen üblichen Methoden eine grosse Zahl von Tetramethylenverbindungen darzustellen, von welchen die folgenden angeführt sein mögen[1]):

Chlortetramethylen,	$\square.Cl$,	Sdp. 85°
Bromtetramethylen,	$\square.Br$,	» 104°
Jodtetramethylen,	$\square.J$,	» 138°
Hydroxytetramethylen,	$\square.OH$	» 123°
Aminotetramethylen,	$\square.NH_2$	» 81°
Tetramethylenaldehyd,	$\square.CHO$	» 117°
Tetramethylenmethylketon,	$\square.CO.CH_3$	» 135°
Tetramethylenphenylketon,	$\square.CO.C_6H_5$	» 259°
Ditetramethylenketon,	$\square.CO.\square$	» 204°
Bromtetramethylencarbonsäure,	$\square(Br).CO_2H$	Schmp. 50°
Hydrotetramethylencarbonsäure,	$\square(OH).CO_2H$,	Sdp. 210° (50 mm)

Auch die drei möglichen Tetramethylendicarbonsäuren,

$$\begin{matrix} CH_2.CH_2 \\ CH_2.C(CO_2H)_2 \\ \textbf{1.1} \end{matrix} \qquad \begin{matrix} CH_2.CH.CO_2H \\ CH_2.CH.CO_2H \\ \textbf{1.2} \end{matrix} \qquad \begin{matrix} CO_2H.CH\langle^{CH_2}_{CH_2}\rangle CH.CO_2H, \\ \textbf{1.3} \end{matrix}$$

sind dargestellt worden.

Die erste derselben wurde erhalten aus Natriummalonester und Trimethylendibromid,

$$CH_2\langle^{CH_2Br}_{CH_2Br} + Na_2C(CO_2C_2H_5)_2$$

$$= CH_2\langle^{CH_2}_{CH_2}\rangle C(CO_2C_2H_5)_2 + 2\,NaBr.$$

und nachträgliche Hydrolyse des Tetramethylendicarbonsäureesters[2]).

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[1]) Perkin, Sinclair, Soc. 61, 37: Perkin, Soc. 65, 950.

[2]) Perkin, Soc. 51, 2.

Sie stellt eine farblose, krystallinische Substanz dar, welche bei 154—156° schmilzt und durch Destillation fast quantitativ in Tetramethylenmonocarbonsäure übergeht:

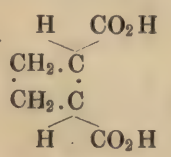
$$\begin{matrix} CH_2.CH_2 \\ CH_2.CH.CO_2H \end{matrix}'$$

die ein unangenehm riechendes Oel vom Sdp. 195° bildet.

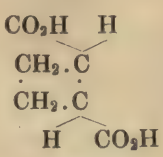
1.2-Tetramethylendicarbonsäure wurde erhalten durch Einwirkung von Brom auf die Dinatriumverbindung des Butantetracarbonsäureesters[1]):

$$\begin{matrix} CH_2.CNa(CO_2C_2H_5)_2 \\ CH_2.CNa(CO_2C_2H_5)_2 \end{matrix} + Br_2 = \begin{matrix} CH_2.C(CO_2C_2H_5)_2 \\ CH_2.C(CO_2C_2H_5)_2 \end{matrix} + 2\,NaBr$$

und nachherige Hydrolyse zur Tetramethylen-1.1.2.2-tetracarbonsäure, welche dann bis zum Aufhören der Kohlensäureentwickelung erhitzt wurde. Diese Dicarbonsäure existirt in wohlcharakterisirten *cis*- und *trans*-Modificationen:



cis-



trans-

vom Schmp. 138° resp. 131°.

Die *cis*-Modification giebt ein Anhydrid (Schmp. 75°) und lässt sich durch Erhitzen mit Salzsäure auf 180° in die *trans*-Säure überführen, welche kein Anhydrid bildet.

Die Tetramethylen-1.3-dicarbonsäure ist von besonderem Interesse, da sie der zuerst dargestellte Abkömmling des Tetramethylens war. Sie wurde von Markownikoff[2]) durch Behandlung von α-Chlorpropionester mit trocknem Natriumäthylat erhalten:

$$\begin{matrix} CO_2C_2H_5.CHCl.CH_3 \\ CH_3.CHCl.CO_2C_2H_5 \end{matrix} = \begin{matrix} CO_2C_2H_5.CH.CH_2 \\ CH_2.CH.CO_2C_2H_5 \end{matrix} + 2\,HCl.$$

Nachher wurde sie auch durch Condensation von Malonester mit Formaldehyd, Hydrolyse des Tetramethylen-1.1.3.3-tetracarbonsäure-

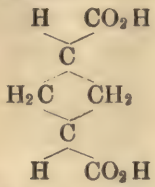
[1]) Perkin, Soc. 51, 21. [2]) Markownikoff, Ann. d. Chem. 208, 333.

esters und darauffolgende Erwärmung bis zum Aufhören der Kohlensäureentwickelung dargestellt[1]):

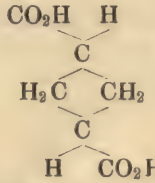
$$(CO_2C_2H_5)_2CH_2 \begin{matrix} CH_2O \\ OCH_2 \end{matrix} H_2C(CO_2C_2H_5)_2$$
$$= (CO_2C_2H_5)_2C<\begin{matrix} CH_2 \\ CH_2 \end{matrix}>C(CO_2C_2H_5)_2 + 2H_2O.$$

$$(CO_2H)_2C<\begin{matrix} CH_2 \\ CH_2 \end{matrix}>C(CO_2H)_2$$
$$= CO_2H.CH<\begin{matrix} CH_2 \\ CH_2 \end{matrix}>CH.CO_2H + 2CO_2.$$

Diese interessante Säure ist gleichfalls in einer *cis*- und *trans*-Modification bekannt:



cis-; Schmp. 135°.



trans-; Schmp. 171°.

Von diesen beiden ist die *trans*-Verbindung schwerer löslich und bildet kein Anhydrid, während die *cis*-Säure leicht in ein Anhydrid vom Schmp. 50° übergeht.

Von den beiden im Vorausgehenden besprochenen Tetramethylendicarbonsäuren ist besonders die 1.2-Säure

$$\begin{matrix} CH_2.CH.CO_2H \\ CH_2.CH.CO_2H \end{matrix}$$

genau untersucht worden. Die erzielten Resultate beanspruchen grösseres Interesse, da sie zur Bildung der einzigen, theilweise ungesättigten Verbindung des Tetramethylens führten, welche bisher erhalten werden konnte[2]).

Wird nämlich das Anhydrid der *cis*-Säure in der üblichen Weise bromirt, so liefert es *cis*-Dibromtetramethylendicarbonsäure,

$$\begin{matrix} CH_2.CBr.CO_2H \\ CH_2.CBr.CO_2H \end{matrix}$$

die bei 202—205° schmilzt und bei Behandlung mit Essigsäureanhydrid leicht in das bei 140° schmelzende Anhydrid übergeht.

Man unterwarf diese Säure ferner der Behandlung mit Kali und hoffte, dass zwei Moleküle Bromwasserstoffsäure austreten würden, unter Bildung von Cyclotetradiëndicarbonsäure:

$$\begin{matrix} CH:C.CO_2H \\ CH:C.CO_2H \end{matrix}$$

[1]) Haworth, Perkin, Soc. 73, 337.
[2]) Perkin, Soc. 65, 581 und 965.

Diese Säure würde die Verbindung des Vierkohlenstoffringes darstellen, welche der Phtälsäure in der Benzolreihe entspräche, und es wäre sehr interessant, festzustellen, ob einer solchen Säure die Eigenschaften einer ungesättigten aliphatischen Säure oder einer Benzolverbindung zukommen würden. Leider vollzieht sich der Reactionsverlauf in ganz anderer Richtung unter Austritt von Kohlensäure und nur eines Moleküls Bromwasserstoffsäure, wodurch Bromcyclotetrencarbonsäure resultirt:

$$\begin{matrix}CH_2.CBrCO_2H\\CH_2.CBrCO_2H\end{matrix} = \begin{matrix}CH_2.C.Br\\CH_2.C.CO_2H\end{matrix} + HBr + CO_2.$$

Ferner wurden Versuche über die Einwirkung von alkoholischem Kali auf Dibromtetramethylendicarbonsäuremethylester angestellt, doch trat dabei alles Brom als solches aus, und erhalten wurde Cyclotetrendicarbonsäure:

$$\begin{matrix}CH_2.CBrCO_2CH_3\\CH_2.CBrCO_2CH_3\end{matrix} \text{ liefert } \begin{matrix}CH_2.C.CO_2H\\CH_2.C.CO_2H\end{matrix}$$

Bald nachher gelangte man fast quantitativ zum Methylester derselben Säure (Schmp. 46°), indem man Dibromtetramethylendicarbonsäureester mit Alkohol und Jodkalium kochte:

$$\begin{matrix}CH_2.CBr.CO_2CH_3\\CH_2.CBr.CO_2CH_3\end{matrix} + 2KJ = \begin{matrix}CH_2.C.CO_2CH_3\\CH_2.C.CO_2CH_3\end{matrix} + J_2 + 2KBr.$$

Cyclotetrendicarbonsäureester schmilzt bei 178° und ist eine sehr beständige Verbindung, welche von Brom nur schwer angegriffen wird. Ihre Eigenschaften lassen die Existenz des theilweise ungesättigten Vierkohlenstoffringes

$$\begin{matrix}CH_2.CH\\CH_2.CH\end{matrix}$$

als möglich erscheinen.

Der Pentamethylenring.

Das grosse Interesse, welches dem fünfgliedrigen Kohlenstoffring zugewendet wird, ist auf die Baeyer'sche Spannungstheorie zurückzuführen, nach welcher der Pentamethylenring,

$$CH_2\begin{matrix}CH_2.CH_2\\CH_2.CH_2\end{matrix}',$$

der am leichtesten zugängliche und der beständigste von allen gesättigten Kohlenstoffringen sein sollte — eine Voraussagung, für deren Richtigkeit mannigfache Beweise erbracht wurden.

Die erste Verbindung des Pentamethylens, welche dargestellt wurde, bildete die Pentamethylen-1.2-dicarbonsäure, welche durch folgende Synthese erhalten worden ist[1]):

[1]) Perkin, Soc. **51**, 244 und **65**, 590.

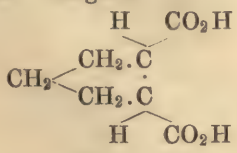
Wirkt Trimethylendibromid auf Natriummalonester ein, so entsteht unter anderem Pentantetracarbonsäureester:

$$(CO_2C_2H_5)_2CHNa + Br.CH_2.CH_2.CH_2Br + NaCH(CO_2C_2H_5)_2$$
$$= (CO_2C_2H_5)_2CH.CH_2.CH_2.CH_2.CH(CO_2C_2H_5)_2 + 2\,NaBr.$$

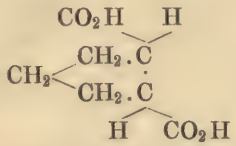
Wird dieser mit Natriumäthylat gemischt und die entstehende Dinatrium-Verbindung dann mit Brom behandelt, so tritt nunmehr eine Ringschliessung ein:

$$CH_2\!<\!\begin{matrix}CH_2.CNa(CO_2C_2H_5)_2\\ CH_2.CNa(CO_2C_2H_5)_2\end{matrix} + Br_2 = CH_2\!<\!\begin{matrix}CH_2.C(CO_2C_2H_5)_2\\ CH_2.C(CO_2C_2H_5)_2\end{matrix} + 2\,NaBr.$$

Der so gebildete Pentamethylentetracarbonsäureester giebt bei der Hydrolyse die entsprechende Säure, welche durch Erhitzen auf 200° unter Kohlensäureentwickelung in Pentamethylen-1.2-dicarbonsäure übergeht. Diese interessante Säure wurde auf diese Weise in ihrer *trans*-Modification erhalten, welche durch Destillation in das Anhydrid der *cis*-Säure übergeht.



cis-; Schmp. 140°.



trans-; Schmp. 160°.

Die Erstere bildet ein Anhydrid (Schmp. 67°) und geht durch Behandlung mit verdünnter Salzsäure bei 180° in die Letztere über.

Einige Jahre später wurde auch das Pentamethylen selbst[1]), sowie eine Anzahl von Verbindungen desselben dargestellt. Die diesbezüglichen synthetischen Methoden wurden bereits besprochen (S. 2096) und führten u. a. zu folgenden Substanzen:

Pentamethylen, , Sdp. 50°

Brompentamethylen, , » 138°

Jodpentamethylen, , » 165°

Ketopentamethylen, , » 130°

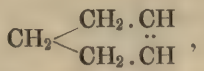
Pentamethylencarbonsäure, , » 215°

Methylpentamethylen, , » 71°

Methylpentamethylencarbonsäure, , » 220°

[1]) Wislicenus, Hentzschel, Ann. d. Chem. 275, 327.

Besondere Erwähnung verdient die Thatsache, dass Wislicenus und Gärtner[1]) sogar zum ungesättigten Kohlenwassersoff Cyclopenten,

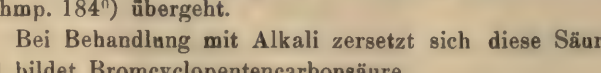


gelangt sind, indem sie Brom- oder Jod-Pentamethylen mit alkoholischem Kali behandelten.

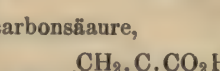
Cyclopenten siedet bei 46° und bildet mit Brom leicht ein Dibromcyclopentan.

Auch Derivate des Cyclopentens wurden auf genau dem gleichen Wege dargestellt, welcher zur Darstellung von Verbindungen des Dihydrocyclotetrens (S. 2118) führte[2]). Das Ausgangsmaterial bildete das *cis*-Pentamethylendicarbonsäureanhydrid (S. 2119), welches bei Einwirkung von Brom glatt in Dibrompentamethylendicarbonsäure (Schmp. 184°) übergeht.

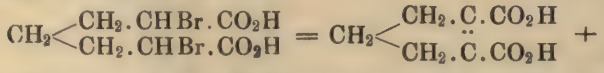
Bei Behandlung mit Alkali zersetzt sich diese Säure sehr leicht und bildet Bromcyclopentencarbonsäure,



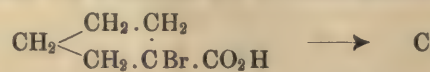
Die Cyclopentendicarbonsäaure,



Schmp. 178°, lässt sich erhalten durch Kochen des Methylesters der Dibrompentamethylendicarbonsäure mit Jodkalium und darauffolgende Hydrolyse oder, wie Willstätter[3]) fand, aus Dibrompimelinsäure mit ätherischer Natriumäthylat-Lösung, wobei die folgende interessante Umsetzung eintritt:



Die entsprechende Cyclopentenmonocarbonsäure wurde durch Einwirkung von Kalilauge auf Brompentamethylencarbonsäure dargestellt.



Sie bildet eine farblose, krystallinische Substanz, welche bei 121° schmilzt und im Aussehen, sowie in ihren Eigenschaften der Benzoësäure sehr ähnlich ist.

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[1]) Wislicenus, Gärtner, Ann. d. Chem. **275**, 331. vergl. Meiser, diese Berichte **32**, 2049 [1899].

[2]) Haworth, Perkin, Soc. **65**, 978.

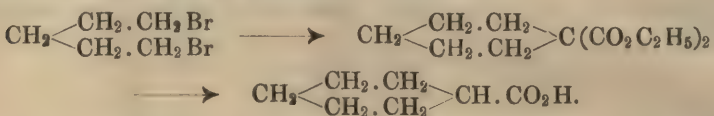
[3]) Willstätter, diese Berichte **28**, 660 [1895].

Hier muss erwähnt werden, dass Krämer und Spilker[1]) im Jahre 1886 aus Steinkohlentheer eine von 160—175° siedende Fraction erhielten, welche ihrer Ansicht nach Dicyclopentadiën enthielt,

$$\begin{array}{l} CH \\ \vdots \\ CH.CH_2.CH.CH.CH_2.CH \end{array}\!\!\!

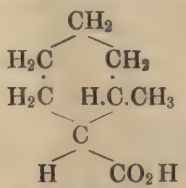
Das reine Hexamethylen schmilzt bei 4.7° und destillirt bei 80.8° [1]). Charakteristisch für den Kohlenwasserstoff ist die leichte Oxydirbarkeit mittels Salpetersäure zu Adipinsäure.

Hexamethylencarbonsäure [2]) lässt sich darstellen durch Einwirkung von Pentamethylendibromid auf Natriummalonester und Hydrolyse und Destillation des so erhaltenen Productes:

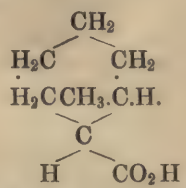


Diese synthetische Säure siedet bei 232—234° und ist offenbar mit der von Aschan [3]) durch Reduction von Benzoësäure erhaltenen Hexahydrobenzoësäure identisch.

Methylhexamethylencarbonsäure wurde ursprünglich in ähnlicher Weise aus Methylpentamethylendibromid und Malonester [4]) synthetisch dargestellt; spätere Untersuchungen [5]) führten zur interessanten Thatsache, dass diese Säure ähnlich wie die Hexamethylendicarbonsäuren in stereoisomeren Modificationen existiert:



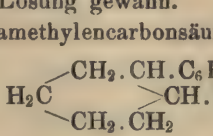
cis-; Sdp. 237°.



trans-; Schmp. 52°, Sdp. 241°.

Die trans-Säure ist aus der cis-Säure durch Erhitzen mit Salzsäure erhältlich und erwies sich als identisch mit der Säure, welche Markownikoff [6]) durch Reduction der *o*-Toluylsäure mittels Natrium in isoamylalkoholischer Lösung gewann.

Die *o*-Phenylhexamethylencarbonsäure,



wurde gleichfalls auf ähnlichem Wege dargestellt [7]), nämlich aus Phenylpentamethylendibromid, $C_6H_5.CHBr.CH_2.CH_2.CH_2.CH_2Br$, und

[1]) Young und Fortey, Soc. **75**, 873.
[2]) Haworth und Perkin, Soc. **65**, 103.
[3]) Aschan, Ann. d. Chem. **271**, 231.
[4]) Freer und Perkin, Soc. **53**. 208.
[5]) Goodwin und Perkin, Soc. **67**, 119.
[6]) Markownikoff, Journ. für prakt. Chem. [2], **49**, 65.
[7]) Kipping und Perkin, Soc. **57**, 306.

Malonester; doch gelang bisher nur die Abscheidung der einen, bei 150° schmelzenden Modification.

Die isomere *p*-Phenylhexahydrobenzoësäure,

$$C_6H_5.CH<\begin{matrix}CH_2.CH_2\\CH_2.CH_2\end{matrix}>CH.CO_2H,$$

welche Baeyer und Rassow[1]) durch Reduction von *p*-Diphenylcarbonsäure erhielten, existirt in zwei stereoisomeren Modificationen von den Schmpp. 180° und 202°.

Zwei Hexamethylendicarbonsäuren, und zwar die 1.3- und 1.4-Dicarbonsäuren, wurden ebenfalls synthetisch dargestellt. Die Erstere[2]) bildet sich aus der Dinatriumverbindung des Pentantetracarbonsäureesters durch Einwirkung von Methylenjodid:

$$CH_2<\begin{matrix}CH_2.CNa(CO_2C_2H_5)_2\\CH_2.CNa(CO_2C_2H_5)_2\end{matrix}\longrightarrow CH_2<\begin{matrix}CH_2\cdot C(CO_2C_2H_5)_2\\ \\CH_2.C(CO_2C_2H_5)_2\end{matrix}>CH_2$$

$$\longrightarrow CH_2<\begin{matrix}CH_2.CH.CO_2H\\ \\CH_2.CH.CO_2H\end{matrix}>CH_2.$$

Sie entsteht dabei in zwei stereoisomeren Modificationen, von welchen die *cis*-Säure bei 163° schmilzt und ein Anhydrid vom Schmp. 189° liefert, während die *trans*-Säure bei 120° schmilzt und kein Anhydrid giebt.

Diese Eigenschaften sind um so überraschender, als im Allgemeinen die *cis*-Modification einer Säure niedrigeren Schmelzpunkt besitzt als die *trans*-Modification, und es ist auch ungewöhnlich, dass das Anhydrid der *cis*-Modification höher schmilzt als die Säure selbst.

Baeyer und Villiger[3]) fanden nachher, dass diese beiden synthetisch dargestellten Säuren mit den *cis*- und *trans*-Hexahydroisophtalsäuren identisch sind, welche sie durch Reduction der Isophtalsäure erhielten.

Hexamethylen-1.4-dicarbonsäure ist ähnlich wie die 1.3-Säure synthetisch dargestellt worden, nämlich aus der Dinatriumverbindung des Butantetracarbonsäureesters und Aethylendibromid[4]):

$$CH_2<\begin{matrix}CH_2.CNa(CO_2C_2H_5)_2\\CNa(CO_2C_2H_5)_2\end{matrix}\longrightarrow CH_2<\begin{matrix}CH_2.C(CO_2C_2H_5)_2\\C(CO_2C_2H_5)_2.CH_2\end{matrix}>CH_2$$

$$\longrightarrow CH_2<\begin{matrix}CH_2\text{——}CH.CO_2H\\ \\CH(CO_2H).CH_2\end{matrix}>CH_2$$

[1]) Baeyer und Rassow, Ann. d. Chem. 282, 139.
[2]) Perkin, Soc. 59, 808.
[3]) Baeyer und Villiger, Ann. d. Chem. 276, 259 [1885].
[4]) Mackenzie und Perkin, Soc. 61, 174.

Die in diesem Falle abgeschiedene *trans*-Säure vom Schmp. 300° wurde identisch gefunden mit der von Baeyer[1]) durch Reduction der Terephtalsäure erhaltenen Hexahydroterephtalsäure.

Cyclische Verbindungen mit mehr als sechs Kohlenstoffatomen.

Es wurden nur wenige Substanzen synthetisch dargestellt, welche sich von Ringen mit mehr als sechs Kohlenstoffatomen ableiten lassen, und diese wenigen wurden in so schlechten Ausbeuten erhalten, dass eine genaue Untersuchung derselben kaum möglich war.

1. Die erste Substanz, welche einen siebengliedrigen Kohlenstoffring enthält und synthetisch hergestellt wurde, ist das Suberon oder Ketocycloheptan, welches in geringer Menge bei der Destillation von korksaurem Calcium entsteht[2]):

$$\begin{matrix}CH_2.CH_2.CH_2.COO\\ CH_2.CH_2.CH_2.COO\end{matrix}\!\!>\!Ca = \begin{matrix}CH_2.CH_2.CH_2\\ CH_2.CH_2.CH_2\end{matrix}\!\!>\!CO + CaCO_3.$$

2. Heptamethylencarbonsäure (Sdp. 248°) entsteht in sehr geringer Menge, wenn das Reactionsproduct von Hexamethylendibromid mit Malonester der Hydrolyse und Destillation unterworfen wird[3]):

$$\begin{matrix}CH_2.CH_2.CH_2Br\\ CH_2.CH_2.CH_2Br\end{matrix} + Na_2C(CO_2C_2H_5)_2 = \begin{matrix}CH_2.CH_2.CH_2\\ CH_2.CH_2.CH_2\end{matrix}\!\!>\!C(CO_2C_2H_5)_2 + 2NaBr$$

$$\begin{matrix}CH_2.CH_2.CH_2\\ CH_2.CH_2.CH_2\end{matrix}\!\!>\!C(CO_2H)_2 = \begin{matrix}CH_2.CH_2.CH_2\\ CH_2.CH_2.CH_2\end{matrix}\!\!>\!CH.CO_2H + CO_2.$$

3. Das einzige Cyclooctanderivat, welches bekannt ist, ist das Ketocyclooctan,

$$\begin{matrix}CH_2.CH_2.CH_2.CH_2\\ CH_2.CH_2.CH_2.CO,\end{matrix}$$

das in minimaler Menge bei der Destillation von azelaïnsaurem Calcium isolirt wurde[4]). Es siedet bei 90—91° (23 mm) und seine Constitution erhellt aus der Thatsache, dass es durch Oxydation in Korksäure übergeht.

---

[1]) Baeyer, diese Berichte 19, 1806 [1886].

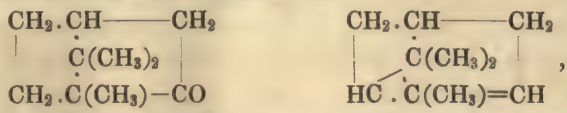
[2]) Boussingault, Ann. d. Chem. 19, 308; Tilley, Ann. d. Chem. 39, 166; Dale und Schorlemmer, Ann. d. Chem. 199, 147; Markownikoff, diese Berichte 25, 26 [1892].

[3]) Haworth und Perkin, Soc. 65, 599; Einhorn und Willstätter, Ann. d. Chem. 280, 140; Willstätter. diese Berichte 31, 2504 [1898].

[4]) Mayer, Ann. d. Chem. 275, 364; Derlon, diese Berichte 31, 1960 [1898]; vergl. auch Müller und Tschitschkin, Ann. d. Chem. 307, 375.

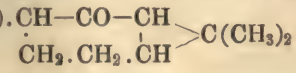
Die synthetische Bildung von bicyclischen Ringen (Ringen mit Brückenbindung).

Die synthetische Bildung von Ringen mit Brückenbindung ist während der letzten Jahre Gegenstand eingehender Untersuchung geworden, und zwar besonders, nachdem gezeigt wurde, dass verschiedene Verbindungen der Terpen- und Campher-Gruppe derartige bicyclische Ringsysteme enthalten. So stellt z. B. Bredt für Campher und Pinen die folgenden Formeln auf:



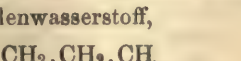
denen zufolge der Campher zwei 5-Kohlenstoffringe, hingegen das Pinen einen 6- und einen 4-Kohlenstoffring enthält.

Ferner gestatten die Untersuchungen von Baeyer und Ipatieff[1]) über die Caronsäure die Annahme, dass die Formel für Caron,



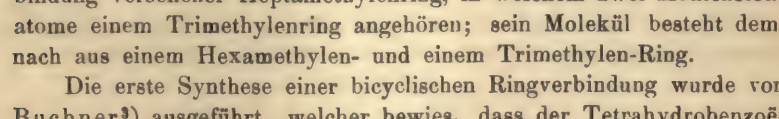
welche zuerst von Wagner[2]) aufgestellt wurde, richtig sei.

Der gesättigte Kohlenwasserstoff,



von dem das Caron sich ableitet, ist somit ein mit einer Brückenbindung versehener Heptamethylenring, in welchem zwei Kohlenstoffatome einem Trimethylenring angehören; sein Molekül besteht demnach aus einem Hexamethylen- und einem Trimethylen-Ring.

Die erste Synthese einer bicyclischen Ringverbindung wurde von Buchner[3]) ausgeführt, welcher bewies, dass der Tetrahydrobenzoësäureester mit Diazoessigester nach der folgenden Gleichung sich verbindet:



und dass die so gebildete Verbindung, welche er wegen ihrer nahen Beziehung zum Caron 1.2-Norcarandicarbonsäureäthylester nennt, einen Heptamethylenring mit Brückenbindung enthält.

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[1]) Diese Berichte 29, 2796 [1896].

[2]) Journ. Russ. Phys.-Chem. Ges. 28, 95 [1896].

[3]) Diese Berichte 33, 3451 [1900].

Während der letzten Jahre haben J. F. Thorpe[1]) und der Vortragende eine Reihe von Versuchen angestellt, um auf synthetischem Wege zu Verbindungen mit brückenartigen Kohlenstoffringen zu gelangen.

Als Ausgangsmaterial wurde die β-β-Dimethylglutarsäure,

$$CO_2H.CH_2.C(CH_3)_2.CH_2.CO_2H,$$

gewählt, da es besonders interessant schien, die Synthese solcher Verbindungen zu versuchen, welche zugleich die für die Campher- und Terpen-Reihe so charakteristische Atomgruppe $.C.C(CH_3)_2.C.$ enthalten. Wird der Ester der Dibromdimethylglutarsäure mit einem Ueberschuss von Natriummalonester behandelt, so vollzieht sich die nachstehende Reactionsfolge:

$$(CH_3)_2C\begin{cases}CHBr.CO_2C_2H_5\\CHBr.CO_2C_2H_5\end{cases} \longrightarrow (CH_3)_2C\begin{cases}C.CO_2C_2H_5\\ \vdots\\C.CO_2C_2H_5\end{cases}$$

$$(CH_3)_2C\begin{cases}C.CO_2C_2H_5\\ \vdots\\C.CO_2C_2H_5\end{cases} + CHNa(CO_2C_2H_5)_2$$

$$= (CH_3)_2C\begin{cases}C(COC_2H_5).CNa(CO_2C_2H_5)_2\\CH.CO_2C_2H_5\end{cases}.$$

Die so erhaltene Natriumverbindung geht, der Behandlung mit Natriumäthylat unterworfen, eine innere Condensation ein unter Bildung der hellgelben und sehr beständigen Natriumverbindung des Dimethylketobicyclopentantricarbonsäureesters[2]):

$$\begin{array}{l}CO_2C_2H_5.C\text{---}C(Na)CO_2C_2H_5\\(CH_3)_2C\begin{cases}|\\CO_2C_2H_5.CH\end{cases}\quad\begin{cases}|\\CO_2C_2H_5\end{cases}\end{array} = \begin{array}{l}CO_2C_2H_5.C\text{---}C(Na)CO_2C_2H_5\\(CH_3)_2C\begin{cases}|\\CO_2C_2H_5.C\end{cases}\quad\begin{cases}|\\CO\end{cases}\\+\ C_2H_5.OH\end{array}$$

Die so entstehende Substanz ist offenbar ein Abkömmling des Bicyclopentan[3]) genannten Kohlenwasserstoffs von der Formel:

$$CH_2\begin{cases}CH.CH_2\\ \vdots\\CH.CH_2\end{cases}$$

Zerlegt man die gelbe Natriumverbindung mit Säuren, so scheidet sich ein farbloses Oel ab, welches ohne Zweifel aus Dimethylketobicyclopentantricarbonsäureäthylester besteht; wird dieser Ester oder seine Natriumverbindung dann mit methylalkoholischer Kalilauge behandelt, so findet eine merkwürdige Zersetzung statt unter Bildung des Kaliumsalzes des Kaliumdimethylketobicyclopentantricarbonsäurediäthylesters:

$$(CH_3)_2C\begin{cases}C(CO_2C_2H_5).CK.CO_2C_2H_5\\ \vdots\quad\quad\quad

Durch Ansäuern derselben wird der freie Ester erhalten, welcher in farblosen, bei 75° schmelzenden Nadeln krystallisirt und bei der Destillation unter Kohlensäureabspaltung in Dimethylketobicyclopentandicarbonsäureester übergeht:

$$(CH_3)_2C<\begin{matrix}C(CO_2C_2H_5).CH.CO_2C_2H_5\\ CH\text{———}CO\end{matrix},$$

ein farbloses Oel, welches unter 30 mm Druck bei 201° siedet und in alkoholischer Lösung mit Eisenchlorid eine starke roth-purpurne Färbung zeigt.

Die freie Säure, welche aus dem Ester durch Hydrolyse mit alkoholischer Kalilauge leicht erhalten werden kann, schmilzt bei 180°; ihre wässrige Lösung zersetzt sich bei 180° unter Kohlensäureentwickelung und Bildung von Dimethylketobicyclopentancarbonsäure (Schmp. 180°):

$$(CH_3)_2C<\begin{matrix}C(CO_2H).CH_2\\ CH\text{———}CO\end{matrix}.$$

Wird hingegen die gelbe Natriumverbindung mit alkoholischer Kalilauge gekocht, so geht sie in eine Mischung zweier stereoisomerer Dimethylketobicyclopentandicarbonsäuren von der Formel:

$$(CH_3)_2C<\begin{matrix}C(CO_2H).CH.CO_2H\\ CH\text{———}CO\end{matrix}$$

über, welche bei 155° resp. 180° schmelzen und mit Eisenchlorid starke Färbung ergeben; die bei 180° schmelzende Verbindung ist identisch mit der vorher erwähnten Säure vom gleichen Schmelzpunkt. Die beiden Säuren ergeben beim Erhitzen unter Kohlensäureabspaltung die Dimethylketobicyclopentancarbonsäure.

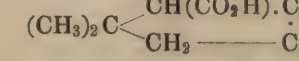
Dieselbe nimmt bei Behandlung mit Natriumamalgam leicht zwei Wasserstoffatome auf und liefert eine Säure von der Formel $C_8H_{12}O_3$ (Schmp. 103°), welche anfangs als die entsprechende Hydroxysäure aufgefasst wurde:

$$(CH_3)_2<\begin{matrix}C(CO_2H).CH_2\\ CH\text{———}CO\end{matrix} + 2H = (CH_3)_2C<\begin{matrix}C(CO_2H).CH_2\\ CH\text{———}CH.OH.\end{matrix}$$

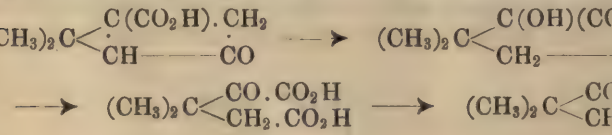
Da jedoch die reducirte Säure ein wohlcharakterisirtes Semicarbazon ergiebt, muss sie offenbar noch eine Ketongruppe besitzen, und diese Thatsache, sowie andere Eigenschaften der Säure sprechen dafür, dass die beiden aufgenommenen Wasserstoffatome den Trimethylenring aufgesprengt haben, bevor noch die Ketongruppe reducirt wurde:

$$(CH_3)_2C<\begin{matrix}C(CO_2H).CH_2\\ CH\text{———}CO\end{matrix} + 2H = (CH_3)_2C<\begin{matrix}CH(CO_2H).CH_2\\ CH_2\text{———}CO.\end{matrix}$$

Die Säure $C_8H_{12}O_3$, welche somit als Dimethylketopentamethylencarbonsäure angesprochen werden darf, wird von Natriumamalgam schwer angegriffen; wird dasselbe jedoch in grossem Ueberschuss angewendet, so findet eine Reduction statt zu Hydroxydimethylpentamethylencarbonsäure (Schmp. 115°):



Durch Salpetersäure wird die Dimethylketobicyclopentancarbonsäure in interessanter Weise oxydirt, indem sie in α,α-Dihydroxydimethylglutarsäure und *gem.*-Dimethyl-Bernsteinsäure übergeht. Dieser Reactionsverlauf, welcher folgendermaassen veranschaulicht werden kann:



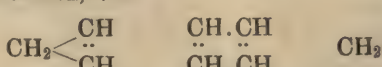
bildet eine werthvolle Bestätigung der angenommenen Constitution dieser bicyclischen Verbindungen.

Es ist zu erhoffen, dass die Fortsetzung dieser Experimente, nach verschiedenen Richtungen hin, nicht nur eine weitere Aufklärung über die Natur der polycyclischen Ringe, sondern auch eine thatsächliche Synthese von Verbindungen ergeben wird, welche den Camphern und Terpenen nahe verwandt sind.

Am Ende meiner Ausführungen angelangt, möchte ich noch Ihre Aufmerksamkeit darauf lenken, dass drei der wichtigsten, mit den geschlossenen Kohlenstoffketten im Zusammenhang stehenden Probleme der weiteren Ausarbeitung harren, nämlich:

I. Die sorgfältige Weitererforschung der Leichtigkeit der Bildung, sowie der Beständigkeit geschlossener Kohlenstoffketten, und

II. Die Herstellung und gründliche Untersuchung von ungesättigten Kohlenwasserstoffen, wie



und deren Derivaten, behufs Feststellung, ob derartige Ringe sich wie gewöhnliche, ungesättigte Verbindungen verhalten, oder ob ihnen Eigenschaften zukommen, ähnlich denjenigen, welche dem Benzolring eigenthümlich sind[1]).

---

[1]) Das Cyclopentadiën ist in neuerer Zeit ziemlich ausführlich untersucht worden; vergl. hierzu Thiele, diese Berichte 33, 666 [1900]; 34, 68 [1901]; Ann. d. Chem. 314, 296 [1901]. Noeldechen, diese Berichte 33, 3348 [1900].

Die Lösung dieser Fragen würde, meiner Ansicht nach, nicht nur über die Ursachen des merkwürdigen Charakters des Benzolringes Klarheit schaffen, sondern würde zugleich unsere Kenntnisse über die Natur des Kohlenstoffatoms selbst erweitern.

III. Die Auffindung weiterer Methoden zur Darstellung von Ringen mit Brückenbindung und besonders die Darstellung von solchen Ringen, welche die Gruppirung $C.C(CH_3)_2.C$ oder $C(CH_3).C(CH_3)_2.C$ enthalten. Bei der Untersuchung solcher synthetischer Ringe wird es jedenfalls möglich werden, die Bedingungen festzustellen, welche zu den merkwürdigen Umlagerungen Anlass geben, die in der Campher- und Terpen-Gruppe so häufig beobachtet worden sind.

Bei der Abfassung dieses Vortrags bin ich von Hrn. Dr. F. Neurath unterstützt worden, wofür ich demselben herzlichen Dank sage.

The Owens College, Manchester.

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